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CHOLECYSTITIS WITHOUT STONES OR JAUNDICE IN ITS RELATION TO CHRONIC PANCREATITIS.

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Cholecystitis without stones is comparatively a common disease, and of late has come into considerable prominence. The types vary in intensity from the mild, chronic catarrhal to those characterized by necrosis of the mucous membrane, perforation, and other manifestations of severe bacterial infection.

A certain amount of uncertainty exists as to when chronic cholecystitis should be considered surgically. Not infrequently the condition is associated with appendicular infections of a chronic character, especially those forms of appendicitis in which foreign bodies, usually fecaliths, are present. Whether or not such appendicular infections are the direct cause of the infections in the gall-bladder has not been determined, but it seems possible inasmuch as bacterial or toxic products are picked up in the derivatives of the portal circulation, carried to the liver, and there destroyed or excreted in a modified form with the bile. When such infected bile is delayed in the gall-bladder, cholecystitis may result.

The clinical diagnosis of cholecystitis even when stones are present is not always easy. With the palm of one's hand, an area may be covered which could be involved in pyloric and doudenal ulcer, disease of the gall-bladder, appendicitis, and stones or infections in the right kidney or right ureter. Pain referred to this region may also be due to small ovarian dermoids and early extra-uterine pregnancy. Frequently the diagnostician must

judge as to the truth of certain alleged facts narrated by the patient not by an examination of the evidence, but by delivering judgment as to the credibility of the statements of the patient. At the time the examination is made, there may be no signs which would furnish a basis of differentiation, since the patient is not then suffering from those leading symptoms which he describes.

If these difficulties present themselves when gall-stones are actually present, how much more difficult is it to make a diagnosis of chronic cholecystitis without stones when signs and symptoms are less marked. Even when the abdomen is open, a gall-bladder markedly diseased in its mucous membrane may give little or no evidence of such disease by external examination. In an examination as to the end results of some 350 patients that had been operated on for gall-stones and cholecystitis, Stanton[1] showed that more than 90 per cent. were cured or satisfactorily improved when gall-stones were present, while in only about 50 per cent. having cholecystitis without stones were the results satisfactory.

Some operators go so far as to say that they never make a diagnosis of gall-stone disease, but tell the patient that he has "an inflamed gall-bladder which needs to be opened and drained." This makes the problem too easy and leads to "snap-shot" judgment in which bias and personal equation assume too much importance. If tarry bile, that is, dark-colored bile containing a considerable admixture of mucus, be accepted as evidence of cholecystitis, a large number of mistakes in diagnosis will not be detected at operation and a corresponding number of patients will fail to obtain relief not because of the failure of operation to cure cholecystitis, but because cholecystitis in the surgical sense was not present. This may also be true of adhesions. It should not be forgotten that so-called bands and adhesions are not limited in their development to fetal life, but are continuously forming throughout life. A band of adhesions frequently extends from the gastrohepatic omentum across the duodenum in its second portion, from the gall-bladder to the transverse colon, without causal infection in the duodenum, gall-bladder, or transverse colon, and, of themselves, such adhesions cannot be considered an indication of cholecystitis. In the later period of life there is often a deposit of fat just underneath the peritoneum of the gall-bladder which gives it a whitish appearance and a feeling of thickness to the touch without any infection of the organ itself, but which may be taken for evidences of cholecystitis. The most reliable sign of cholecystitis is markedly enlarged glands along the common duct and at the juncture between the common and cystic ducts. In cholecystitis of long standing, such lymph nodes may become calcareous. Two cases of chronic cholecystitis

[1] Jour. Amer. Med. Assoc., August 5, 1911, pp. 441–4.

were observed in our clinic in which calcareous lymph nodes compressed the common duct, producing jaundice. In both instances the patients were cured by the removal of the gall-bladder and the obstructing glands.

Chronic cholecystitis produces two types of gall-bladders: (1) The large, blue, distended gall-bladder, which does not empty itself normally under compression. The bile in the gall-bladder is thin and often foul-smelling from colon infection. (2) The thick-walled, whitish gall-bladder, which is often adherent, and contains bile usually thick and tarry, with a large admixture of mucus. In many instances the gall-bladder appears to be normal. As a rule, enlarged glands along the common duct will readily be detected. Enlargement of the lymphatics may be the only sign in some cases to indicate that the gall-bladder is probably diseased. If the symptomatic evidence that cholecystitis is present is characteristic, it becomes necessary to open the gall-bladder and examine the mucosa before a diagnosis can be definitely established. At times the disease will be limited to one area which will probably not be detected by merely opening and examining the mucous membrane. In such cases the cause of the symptoms may not be discovered unless the entire gall-bladder is removed and subjected to careful scrutiny.

Assuming the foregoing to be true, it can readily be seen that while cholecystitis without gall-stones exists, until the gall-bladder is opened its existence cannot always be determined. Even after opening the gall-bladder and exposing the mucous membrane, the diagnosis of cholecystitis in the surgical sense may remain more or less doubtful until the gall-bladder or some portion of its mucous membrane be subjected to examination by the pathologist. Fortunately, for purposes of diagnosis, the strawberry gall-bladder is one of the more frequent types of cholecystitis, the mucous membrane being covered with yellow specks as though from ulceration and deposit of gall-stone material. As a matter of fact, these little yellow specks are the base of the exposed villi of the mucous membrane, which have been strippped of their covering epithelium and their connective tissue has been stained yellow by the bile.[2] The disease is strictly confined to the gall-bladder. The strawberry gall-bladder is easily diagnosed on inspection of the mucous membrane. Following radical operations for this condition as high, if not higher, percentages of cures are obtained as following radical operations for gall-stones, because the common and hepatic ducts, if involved at all, will be involved only in a catarrhal process and not subjected to the traumatism of possible stones which have descended from the gall-bladder into these ducts.

Taking the strawberry gall-bladder as the type, the more varia-

[2] MacCarty: Annals of Surgery, May, 1910, pp. 651–669.

tion from it toward the normal gall-bladder the less the prospect of cure following operation because of less certainty in the diagnosis. Our scientific conscience should not be satisfied by asserting, on slender evidence, that cholecystitis exists if a diagnosis of gall-stones has been made and stones have not been found. The wish may be father to the thought and the condition should not be pronounced cholecystitis without such a diagnosis being verified by the pathologist and a grade of severity established which would make it a surgical disease. We all experience humiliation on failing to verify, at operation, a diagnosis of gall-stone disease or cholecystitis. These failures should be classified and recorded in the hospital statistics as "negative explorations of the gall-bladder." In the present state of our knowledge these are justifiable mistakes.

The milder degree of cholecystitis when subjected to operation will not present a high percentage of cures, and under existing conditions should usually be considered medical rather than surgical.

Experience teaches another lesson. While cholecystotomy may be an efficient procedure in gall-stone disease when the gall-bladder is otherwise normal and the ducts are free, in cholecystitis the method is not satisfactory. A gall-bladder which can keep up continuous trouble from infection alone without the mechanic irritation of gall-stones will probably not be cured by simple drainage, and cholecystectomy will be the procedure to follow. As a matter of fact, cholecystectomy is now largely indicated in gall-stone disease, and it may be said that practically all cases of cholecystitis and the large majority (probably 80 per cent.) of cases of gall-stone disease should be treated by cholecystectomy rather than cholecystostomy.

If so much uncertainty can exist with regard to the gall-bladder and its infections, how much more uncertainty must exist as regards the pancreas and its infections. The sense of sight cannot aid in solving the question, as in the examination of the mucosa of the gall-bladder, and a specimen will probably not be removed for pathological examination. The diagnosis must be established by the sense of touch and a certain amount of "intuition" on the part of the diagnostician, which unfortunately often plays too large a part in his final judgment. For many years I have made it a practice to examine the entire contents of the abdomen with the gloved hand whenever it was opened for any purpose and the condition of the patient would permit such manipulation. I have been surprised to find how frequently the pancreas showed enlargement, induration, and nodulation which would have justified a diagnosis of chronic pancreatitis if some disease of the biliary tract had been the original lesion, but in which there was no symptomatic evidence whatsoever that pancreatic inflammation existed.

In the routine examination of patients in our clinic, several hundreds of examinations of the stool have been made, in cases of chronic pancreatitis of this type, to try and ascertain whether or not there were symptoms of pancreatic insufficiency. Such a condition was rarely shown either in cholecystitis or in connection with gall-stone disease. It would seem, therefore, that statistics of the relative frequency of chronic pancreatitis should be accepted with some reserve. Evidence which to one would indicate chronic pancreatitis, to another might not do so. Yet that chronic pancreatitis does exist, and that it exists most commonly in connection with infections of the biliary tract, is an established fact.

The well-marked cases of chronic interlobular pancreatitis involving the head and often the entire pancreas, present conclusive evidence of pancreatitis just as the strawberry gall-bladder presents conclusive evidence of cholecystitis. Such extreme evidence of chronic pancreatitis is seldom found without infection of the biliary tract, but in cases less marked the evidence is often insufficient to establish the diagnosis, especially when neither gall-stones nor jaundice are present.

Robson[3] has shown that in one-third of the cases the common duct passes behind the pancreas, so that even if chronic pancreatitis is present, the common duct is not necessarily compressed and there may be no jaundice. In such cases, however, an infection from the biliary tract may extend to the pancreas and produce chronic pancreatitis. Whether this occurs more often by mucus continuity through the cystic, common, and pancreatic ducts, or, as Deaver[4] has shown, through the associated lymphatics, cannot always be determined.

Estimating at their full value all of these possible sources of exaggeration or error, there still remains a group of cases in which cholecystitis of a chronic type without gall-stones and without jaundice is accompanied by undoubted chronic interlobular pancreatitis. In such cases there is no dilatation of the common duct nor is the gall-bladder distended. That chronic pancreatitis is best treated by drainage of the bile tract is a lesson so thoroughly taught that even in those cases in which there is no evidence whatsoever of interference with biliary or pancreatic drainage, as shown by jaundice and distention of the common duct and gall-bladder, we still adhere to the practice of draining the gall-bladder without regard to the fact that it is the infection within the gall-bladder which has caused the disease of the pancreas, and that this infection will probably not be cured by drainage.

It is the object of this paper to show that in the presence of chronic pancreatitis without jaundice and without evidences of

[3] Diseases of the Gall-bladder and Bile Duct, 1904.
[4] Deaver: Annals of Surgery, xxiv, 1896, pp. 58–63.

back pressure on the biliary tract the gall-bladder should be removed if it shows marked evidences of chronic cholecystitis, especially the strawberry type.

In at least a half-dozen cases operated on in our clinic the following sequence has occurred: Cholecystostomy had been done for chronic cholecystitis without stones, and with a complicating chronic pancreatitis. The patient was relieved for some weeks or months and then the symptoms returned. Recognizing the need of more prolonged drainage, the gall-bladder was reopened and drained for a considerable period. There was complete relief so long as drainage of the gall-bladder continued, but sooner or later, after the fistula in the gall-bladder healed, the symptoms returned.

These cases are characteristic, and I have no doubt have been observed by many surgeons who have been puzzled to know just what course to pursue. It has been our experience that removal of the gall-bladder promptly relieves the symptoms and permanently cures the patient. Just what the future condition of the pancreas may be, one has no means of knowing, but I have found that chronic pancreatitis, the result of gall-stone disease, is usually cured by the removal of the stones and drainage of the biliary tract, and that in the chronic infections of the gall-bladder with secondary involvement of the pancreas, in the absence of interference with biliary drainage, cholecystectomy furnishes a satisfactory symptomatic cure.

THE TREATMENT OF PYLOROSPASM IN INFANCY.

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As early as 1788 Hezekiah Beardsley described a condition of stenosis and thickening of the pylorus occurring in young infants, and during the middle of the last century, Williamson and Dwosky also published accounts of this disease; but attention was not directed to it with sufficient force to bring it to the notice of the profession in general until Hirshsprung studied it in 1888. Since that date there have been a large number of contributions on this subject and an immense amount of theorizing as to the cause of this and allied conditions.

There is a symptom-complex not infrequently met with which is so striking that it cannot escape attention. This consists in vomiting, which is more or less projected in character, and con-

sisting of food, some mucus, and at times streaks of blood. There is constipation, or sometimes alternating constipation and diarrhea, loss of weight, a dilated stomach, visible peristalsis, and in many cases careful palpation reveals a thickened pylorus. This symptom-complex, with slight variations, may be caused by two conditions, one which may be and usually is called congenital hypertrophic pyloric stenosis, and the second pylorospasm.

The first of these conditions has been noted in autopsies of the fetus, and has been studied in autopsies on infants. It is distinctly a congenital condition, concerning which there is considerable difference of opinion. It occurs in all classes of society, affects the firstborn more frequently than any other child, and there is rarely but one instance in one family. Eighty per cent. of the cases occur in boys. The symptoms in these cases date from birth or shortly after birth.

Pylorospasm, on the other hand, may be regarded more as an acquired condition, may occur either in breast-fed or artificially fed infants, and while commonly seen from one to two weeks after birth, may be noted at any age. Pylorospasm we know chiefly by its symptomatology and the study of the living cases. There are gradations between these two classes, so that a mild case of the congenital form may have associated with it a considerable amount of spasm which intensifies the symptoms, and, on the other hand, it seems highly probable that a more or less continuous spasm of the pylorus might lead to thickening of the pyloric muscle, just as increased use of any muscle leads to hypertrophy. The outlook in these two conditions varies greatly. The well-marked cases of hypertrophic stenosis are exceedingly liable to die unless an operation is performed which will permit food to pass from the stomach, otherwise the child gradually starves to death. The pure cases of pylorospasm, particularly those coming on in late infancy, almost invariably get well, if properly treated; but there are certain cases which go on to an unfavorable termination regardless of the management.

With our present knowledge it would seem impossible to tell in every instance whether the lesion was distinctly congenital or whether it was acquired after birth. The important point from the standpoint of prognosis and treatment is to differentiate the cases in which there has been a great amount of thickening and those in which the condition is largely, if not entirely, due to spasm. This differential diagnosis cannot always be made, but there are a certain number of things which help one in making the decision. In the cases in which there is actual stenosis and thickening, the infants are constipated and the stools may even be of a character suggesting starvation. The vomiting may begin shortly after the birth of the child, and is usually, though not always, sometime after taking the feeding. The emaciation is

progressive, visible peristalsis very marked, and in most instances the enlarged pylorus is felt without any difficulty. It is a hard, unchanging mass. In the pylorospasm cases, on the other hand, there are alternating periods of constipation and diarrhea, the vomiting is usually, although not always, immediately after taking food, the visible peristalsis is not so marked, and a tumor at the site of the pylorus may or may not be felt. In some instances the tumor is felt only with peristalsis, and it may change in its size and shape under the palpating finger; when this occurs it is safe to make the diagnosis of pylorospasm, or at any rate the condition consists of much more spasm than it does of actual thickening. The pylorospasm may occur at any age. It does not always follow so definitely after birth. I have had one instance, however, in which the vomiting dated almost immediately from birth, the child subsequently making a perfect recovery.

The question of the management of these cases is one of great importance. The first point to consider is the advisability of operative procedure, and while this should be undertaken in undoubted cases of hypertrophic stenosis, and the chances of recovery of the child are better if it is not postponed too long, still in view of clinical experience with these cases, the writer thinks one should always go slowly in deciding whether one is dealing with an hypertrophy or a pylorospasm. In a certain proportion of cases in which the lesion is apparently an hypertrophic stenosis, recovery takes place without operation. Every case must be decided on its own merits, according to existing conditions. A period of from three to six weeks of medical treatment may be tried before deciding upon an operation, unless all the symptoms and signs should make the diagnosis perfectly clear before this period has elapsed. This period of waiting will generally make clear if not the actual condition, certainly the severity of it. Cases coming on immediately after birth and severe in character are much more likely to require operative interference than those which come on later and progress more slowly. The choice of operation lies between a pyloroplasty and a posterior gastro-enterostomy, and this decision may be left to the operating surgeon.

The management of these cases from the medical standpoint is extremely important. The first point of importance is the feeding and there can be no question whatever that these patients, and we refer particularly to pylorospasm, do better on breast milk than upon any other food that can be found. In severe cases occurring in young infants every effort should be made to obtain human milk. This point cannot be emphasized too strongly. If the mother's milk contains a great deal of fat, it may be allowed to stand and some or all of the cream removed. There is considerable difference of opinion as to the effect of the fats in feeding these cases, and it seems to me there is considerable variation in the cases in regard to this. If the case is not doing well, it certainly

is not amiss to remove the fat, at least temporarily. I should not consider using any other form of feeding than human milk or some slight modification of it unless circumstances absolutely prevent securing it. When it cannot be obtained in sufficient quantities, more or less completely peptonized cow's milk may be substituted for part of the feeding. This milk may be one part cow's milk and three parts water, or one-third cow's milk and two-thirds water, peptonized from five to twelve minutes, or the weaker percentages of modified milk may be used; if these fail, well-diluted malted milk or condensed milk diluted with water, in a proportion of one to ten or one to twelve may be tried. In the severe cases in which practically everything is vomited, the food should be given by means of a stomach-tube, as it is much more liable to be retained when given in this way than if the baby be allowed to nurse the breast or to take the milk from a bottle. There are curious things in regard to the retention of food, two of which deserve special mention: one is that with any change of food there is retention of the food for two or more feedings, and sometimes eight, twelve, or sixteen hours elapse before the vomiting recommences. The second point is that sometimes several feedings are taken one after the other, the stomach becoming more and more dilated, and finally the total quantity of food vomited hours afterward. The use of the tube for feeding obviates putting milk into an already filled stomach. The frequency of feeding is a matter of considerable importance, and will depend upon the amount that can be given. Most of these babies will retain small feedings longer than larger ones, but I think it is a good plan to gradually increase the size of the feeding, giving as much as can be retained. If the feeding is a little too large it will be rejected, but a competent nurse can usually determine the size of the feeding after a little experience with any given child. Two hours should perhaps be the greatest interval that should be allowed to elapse between the feedings, and in some cases this interval may be shortened to considerable advantage. Occasionally, longer intervals may be resorted to temporarily, but not as a general rule. The child should be kept flat on its back immediately after the feeding, and not handled any more than is absolutely necessary. In this connection it is hardly necessary to add that the child should be kept in a perfectly quiet room and not disturbed by visitors and friends or any other members of the family.

The stomach should be washed out once or twice a day or oftener, varying the frequency of the lavage according to the amount of mucus present, and it is sometimes advisable to use a bicarbonate of soda solution, one dram to the pint, in cases where the mucus is thick and stringy or where the vomitus is intensely acid. Other foods than those mentioned above have been suggested, particularly beef-juice and the white of egg and water, or the use of cow's milk with sodium citrate. The meat and the egg we should

regard as doubtful expedients, as neither is adapted for more than the most temporary feeding, and even that on a starvation basis. Rectal feeding may be used in bad cases, but in my experience the administration of food by rectum in young infants is not a satisfactory method of feeding, although there is no doubt that even the small amount that can be thus given and absorbed is of distinct value. The use of the rectal administration of plain water or in some instances of salt solution is, however, of the greatest benefit, and may be used in all cases where the amount of fluid vomited is very great. It relieves the thirst of the child and stimulates excretion of the urine.

Another point of importance is to maintain the body heat. The temperature of the child should be taken and hot-water bags or other devices used as may be necessary. Occasionally there may be a certain amount of febrile disturbance, particularly when the starvation begins to be manifest.

Counter-irritation over the epigastrium has been suggested, particularly by German writers, and this is usually accomplished by means of weak mustard plasters, spice bags, or by some form of a warm application. Too much need not be expected from this procedure, but there is no reason why it should not be tried.

The question of the use of drugs in these cases is one about which there has been considerable written. In my experience, atropin is so far superior to any other form of medication, and I unhesitatingly recommend it as the first thing to try, giving it in doses of $\frac{1}{2000}$ grain at intervals of four to six hours, and sometimes even at shorter intervals. This dose may be reduced if it produces symptoms of belladonna poisoning, but I have never seen this amount cause any such trouble. If no therapeutic effect is obtained after a reasonable trial, the dose may be cautiously increased until the first symptoms of the drug are noted. As soon as this is seen, the amount may be diminished and the smaller doses, if found useful, may be continued even over a considerable length of time. Opium in the form of the deodorized tincture has its warm advocates. Codein may be tried in place of opium. When codein is used, $\frac{1}{600}$ grain may be administered at the start, and the amount increased cautiously. If the deodorized tincture is preferred, $\frac{1}{40}$ minim may be the starting dose. Sodium citrate, bismuth subnitrate or other bismuth preparations, alkalies, and acids have all been suggested, but are of exceedingly questionable value.

SUMMARY. The points to which I have particularly called attention are:

1. A more careful diagnosis.
2. A longer trial at medical treatment, especially in all cases in which the diagnosis of pylorospasm is probable.
3. The necessity of the use of breast milk.
4. The superiority of atropin to other forms of medication.

TUBERCULOSIS OF THE SPLEEN, SEPTIC INFARCTION, POLYCYTHEMIA, SPLENECTOMY.

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Secondary tuberculosis of the spleen is not uncommon. True primary tuberculosis of the spleen is probably extremely rare. In the cases of so-called primary tuberculosis of the spleen described in the literature the tuberculous process in the spleen forms the main lesion, the probable original focus or point of entry, in the lungs or lymph nodes, for example, remaining quiescent or becoming healed, while the process in the spleen develops, and is the cause of the symptoms presented by the patient.

The first case of primary tuberculosis of the spleen was reported from autopsy by Coley[1] in 1846. The first reported splenectomy for splenic tuberculosis is that of Burke[2] in 1889. The patient died the following day, apparently from sepsis. No autopsy was performed in this case, but previous physical and sputum examination showed no evidence of pulmonary tuberculosis. In 1898 Quenu and Baudet[3] collected and reported five cases, including one of their own. In 1899 Rendu and Widal[4] described a symptom-complex including tuberculosis of the spleen, polycythemia without leukemia, and cyanosis. They attributed the symptom-complex to the splenic lesion. Bayer[5] collected, up to 1900, 9 operations with 7 recoveries, including 1 of his own, and 19 autopsy cases. He emphasizes the importance of splenectomy, and also the relative diagnostic importance of polycythemia and cyanosis. His patient had 6,000,000 red cells, 7500 white cells, hemoglobin 40 per cent., and was pale. G. B. Johnson[6] in an article on splenectomy published in 1908 included reports of ten cases of splenectomy for tuberculosis, with two deaths.

The most recent and complete article on this subject is that by Winternitz,[7] who has collected and tabulated 51 cases from the literature; 16 of these cases have been operated on, 9 cases recovered (56 per cent.). The list includes 3 cases; 1 by Ciaccio,[8] in which

[1] Trans. Path. Soc., London, 1846, i, 276.
[2] Dublin Jour. Med. Sci., 1889, xlvii, 540.
[3] Rev. de gynec. et de chir. abd., 1898, ii, 317.
[4] Bull. et mém. Soc. de Med. des hôp., 1899, Series 3, xvi, 528.
[5] Mitt. a. d. Grenzgeb. d. med. u. chir., 1904, xiii, 523.
[6] Ann. of Surg., 1908, xlviii, 50.
[7] Archiv Int. Med., 1912, ix, 680.
[8] Deutch. Zeitsch. f. Chir., 1909, lviii, 464.

splenectomy was not done on account of adhesions; 1 by Hayden,[9] in which the spleen was sewed to the abdominal wall and drained; and 1 by Hamilton,[10] in which the same procedure was carried out. His analysis and summary of the 51 cases is so thorough and complete that the conclusions found as a result of his study may be given here as follows:

Tuberculosis of the spleen seems to be equally frequent in the male and female sex. It is most frequent between the ages of twenty and forty, but may occur at any age, the youngest in his tabulated list being one year, the oldest eighty years. The symptoms may run an acute or chronic course, in the acute cases the symptoms were those of an acute systemic infection, and in the chronic cases the onset was characterized by pain or tumor in the splenic region (70 per cent. of cases). There may be, in addition, gastro-intestinal or respiratory disturbances. In the list of 51 reported cases the blood count was given in 26. It was normal in 9 (34.61 per cent.), and showed anemia in 11 (42.30 per cent.); polycythemia was present in 6 (23.08 per cent.). The anemia was not marked in any instance, 3,200,000 being the lowest count. As a rule the leukocytes were not increased, and their number seems totally independent of the number of red cells. In his conclusion, Winternitz states that "death invariably follows if the spleen is not removed."

In contrast to this statement of Winternitz we have the statement of Osler[11] in an article on Erythrocythemia, "Splenectomy should never be done in these cases." And the list of reported cases in which the blood picture shows a true polycythemia bears out this latter conclusion. In view of the fact that in our case tuberculosis of the spleen and polycythemia co-existed, these conflicting statements make the question of the treatment of such cases a difficult one. Owing to the apparent relationship between tuberculosis of the spleen and polycythemia it may be of interest in this place to consider briefly what is known of polycythemia, excluding those cases due to change in altitude or chronic coal-tar products poisoning:

Polycythemia as a definite disease was first described by Vaques[12] in 1892. Osler[13] in 1903 and Turk[14] in 1904 brought the syndrome into general notice (enlarged spleen, cyanosis, and high red-count), with early case reports by McKeen[15] and Saundby and Russell.[16] Since then so many cases have been reported in the literature that in 1911 Watson Wemyss,[17] in a review of the subject, cites sixty references.

[9] Trans. Indiana State Med. Soc., 1897, xlviii, 96.
[10] Internat. Clin., 1896, vi, Series 3, 213.
[11] Principles and Practice of Medicine, 1912, Eighth edition, 757.
[12] Compt. rend. Soc. de biol., Paris, 1892, xliv, 384.
[13] Amer. Jour. Med. Sci., 1903, cxxvi, 187.
[14] Wien. klin. Woch., 1904, xvi, 153.
[15] Boston Med. and Surg. Jour., 1901, 144.
[16] Lancet, 1901, i, 515.
[17] Edinburgh Med. Jour., 1911, vol. vi.

There are five theories as to the etiology of polycythemia: (1) That the disease is a primary myelopathy (Parks Weber),[18] and Jacobs[19] writes of the disease as a neoplasm of the blood similar to a neoplasm of the tissues in cancer; (2) splenic tuberculosis (Rendu and Widal[20] and Lefas);[21] (3) diminished destructibility of the red blood corpuscles; (4) diminished oxygen-carrying power of the hemoglobin (Bence);[22] (5) theory of blood-stasis, the extreme viscosity of the blood being a marked phenomenon in these cases of polycythemia.

The above brief review of the literature on the subject is enough to indicate how little really has been definitely determined as to the etiology and essential pathology of polycythemia. Moreover, the direct relation between polycythemia and tuberculosis of the spleen is open to question. Therefore, while the multiplicity of lesions demonstrated by autopsy, in the following case, prevents definite conclusions, the history, report of operation, clinical data, and report of autopsy are presented as a contribution to the literature on the subject.

For much of the previous history of this patient, and for the clinical data extending over a period of seven years, we are indebted to Dr. J. A. Travell, of New York.

CASE I.—J. R. S., aged thirty-nine years; salesman; born in United States.

Family History. Mother died of nephritis, otherwise irrelevant.

Previous History. Had chills and fever when a child; in youth had frequent severe nose-bleed, but in 1901 an operation for abscess in the inguinal region was not accompanied by unusual bleeding. In 1902 had pneumonia, followed by pleurisy. Was formerly a hard drinker, but later a total abstainer. Had always been constipated. Normal weight was about 180 pounds.

History taken in 1905 stated that there had been no recent cough, catarrh, or pleurisy. During the previous year he had begun to have frequent attacks, in which his face turned purple, and he became nervous, but never lost consciousness. At that time he was recovering from an attack of nervous prostration, and was troubled with indigestion and spots which flickered before his eyes. He, however, had no headache. Weight was then 147½ pounds. Physical examination showed right kidney palpable; heart lungs, and urine normal; face flushed. Intense congestion of all mucous membranes, but legs and body pale.

January, 1907. For a period of three weeks had had momentary attacks of complete blindness of the right eye from one to six times a day. An oculist reported the eyes were normal and that the

[18] Quarterly Jour. Med., 1908, vol. ii.
[19] Münch. med. Woch., 1912, lix, No. 44.
[20] Loc. cit.
[21] Paris Thesis, 1903.
[22] Deutsch. med. Woch., 1906, xxxii, 1451.

trouble was due to vasomotor disturbance. All capillaries of the body were intensely congested. Was always constipated.

April 6, 1908. Extreme capillary congestion of the face and mucous membrane of the mouth. Color below the neck was normal; feet were cool. Had epigastric pain at times, with gas in the stomach. Heart was normal; radial and temporal arteries were hard. Spleen was palpable one inch below ribs on deep inspiration.

April 8. A gall-stone was passed after severe pain for twenty-four hours. Stone was not recovered. Hemoglobin, 90 per cent.; polynuclear leukocytes, 88 per cent.; transition leukocytes, 1 per cent.; eosinophiles, 2 per cent.; small lymphocytes, 5 per cent.; large lymphocytes, 4 per cent.

April 22. Face was flushed as usual. Abdomen was not sensitive. Liver dulness was normal. Spleen was not palpable.

May. Face was scarlet. Spleen was barely palpable below the ribs. No hepatic tenderness; no gastric splashing. Drinking buttermilk invariably caused blindness and dizziness in half an hour, the attack lasting twenty minutes.

June. Face was constantly flushed; weight, 146½ pounds. Spleen not palpable; heart, lungs, and abdomen were negative. Reflexes were present; blood-pressure, 140 mm.

July. Spleen not palpable, lacked ability to concentrate attention on work. Face was scarlet.

January, 1909. Had been well, but had frequent lapses of memory, and the face flushed annoyingly.

February. Urine examination showed albumin, acid; no sugar; granular and hyaline casts; many pus cells and spermatozoa. Quantity, two quarts in twenty-four hours. Pulse, 93 and regular, blood-pressure, 130 mm. Marked gastric splashing.

March. Had severe hemorrhage; about one quart from the bowels, immediately followed by about one quart from the stomach; both clotted heavily. Collapse; pulseless; soreness at lower left border of the stomach. The following day pulse was regular, of fair quality. No further hemorrhage. Urine, ninety-six ounces in twenty-four hours. No sugar, no albumin, many casts. Two days later the blood-pressure was 140 mm.

April. Frequent neuralgic pains in superficial vessels of the calves of the legs, lasting about five minutes. Veins distended. Face flushed, and dizzy at times. Blood-pressure, 110 mm. Weight, 145½ pounds.

May. Felt well; passed about three quarts of urine in twenty-four hours.

August. Face and hands flushed and cyanotic. Blood-pressure, 130 mm. Gastric splashing. Often lost control of himself. Slept poorly.

October. Had felt unusually well for some time. Blood-pressure,

135 mm.; weight, 152½ pounds. When badly constipated had spells, during which he momentarily lost consciousness.

June, 1910. Departed for the West. Had a good year and, as a rule, felt well. Blood-pressure, 140 mm. Heart and lungs were negative. No aneurysm. Urine showed trace of albumin; much indican. Not any blind spells.

October. While in Portland, Oregon, the patient had another severe hemorrhage, both from the stomach and bowels, and came under the care of Drs. J. O. E. King and Jones, of Portland. After this attack a careful clinical examination was made of stomach contents, stools, and blood. The gastric analysis and stool examination were negative. Blood-pressure was between 100 and 120. Leukocytes, 32,000; red cells, 6,000,000. Weight, 148 pounds. During the interval between this attack and the year 1912 he remained in the West and did no work on account of his health. He was bled once, with relief of his symptoms. While in the Battle Creek Sanatorium during this time his blood examination was red cells, 6,550,000; hemoglobin, 92 per cent.; leukocytes, 41,000. Percentage of polynuclear cells was not given. His blood-pressure was then about 120.

In the spring of 1912 he returned to New York and resumed his occupation, and reported himself in fairly good health. Six weeks before his admission to St. Luke's Hospital, November 27, 1912, he had been suffering with indigestion and some pain in the region of the spleen. He stated that eight days before, while on a business trip, after a ride of thirty miles in a wagon on two successive days over rough roads, this pain became more severe, extending to the epigastrium. Everything he ate caused excruciating pain. He did not vomit, but felt nauseated. For several days his bowels did not move. He was then seen by Dr. Egbert Le Fevre, of New York. His chief complaints at this time were severe pain in the left hypochondriac region, radiating toward the midline and across the abdomen, extreme weakness, and a feeling of fulness in the head. His temperature was 101°.

Physical Examination. The physical examination of the lungs was negative. There was an indistinct systolic murmur at the apex. Pulse in the right radial only slightly above normal in rate. Pulse in left radial absent. The spleen was palpable about three inches below the free border of the ribs, and extremely tender. A blood-count showed between 30,000 and 40,000 leukocytes, with 92 per cent. of polynuclear cells. Two days later he was seen in consultation by one of us, his condition having remained the same, except for an increased elevation of temperature and extreme difficulty in moving the bowels (only once in three days). He was then referred to St. Luke's Hospital for observation. His temperature on admission was 103°; pulse, 100; respiration, 26. His leukocytes were 23,000; polynuclear cells, 92 per cent.

At 10 P.M. on the night of admission he had a severe chill, and one hour later his temperature was 105.3°; pulse, 148; respiration, 34. Leukocytes, 39,000; polynuclears, 95 per cent. His urine showed albumin, leukocytes, and a few red cells. Believing that he had an abscess or some septic process in the spleen, an immediate operation was advised.

Operation. An incision about 20 cm. long was made along the outer border of the left rectus muscle, and the spleen was found studded with small white areas which looked like tubercles or miliary abscesses; there was also a large softened area, evidently an infarction. The spleen was only moderately adherent, and no tubercles were seen elsewhere in the peritoneum. The liver was apparently normal. A splenectomy was done with little difficulty. The lower end of the wound was closed, the upper part being left open to allow the packing and drainage with a Mikulicz drain of the upper part of the space left by removal of the spleen, from which there was a moderate amount of oozing caused by separation of the adhesions.

For the first four days following the operation the patient's temperature averaged from 100.2 to 101.4; pulse, 116 to 128; respiration, 32 to 48. Urine showed albumin and casts. Blood picture: Red blood cells, 8,800,000; hemoglobin, 120 per cent.; white blood cells, 80,000; polynuclears, 96 per cent. A few normoblasts were found, and also aniso- and poikilocytosis and polychromatophilia.

On the fifth day the patient appeared better. Temperature, 100° to 102.2°; pulse, 116 to 128; respiration, 30 to 36; red blood cells, 7,000,000; hemoglobin, 120 per cent.; white blood cells, 21,300; polynuclears, 92 per cent.; three normoblasts in two hundred cells. Bowels moved twice.

On the sixth and seventh days the general condition about the same. Blood pressure, 117. Wound dressed, and appeared in good condition. Packing removed and a rubber dam drain inserted.

On the eighth day the temperature in the morning was 100.4°; pulse, 116; blood-pressure, 118; red blood cells, 7,600,000; hemoglobin, 120+ per cent.; white blood cells, 18,000; polynuclears, 96 per cent.; five normoblasts in one hundred cells. In the evening the patient complained of abdominal pain and felt chilly. At midnight the temperature was 100.4°; pulse, 148.

December 6, the ninth day after operation, patient's condition was worse. Temperature, 104.4°. Complained of severe abdominal pain; vomited at noon. Red blood cells, 7,400,000; hemoglobin, 120 per cent; white blood cells, 23,000; polynuclears, 88 per cent. In the evening he rapidly became worse; his pulse became almost imperceptible. Rallied after intravenous infusion of saline solution. Asked for bed-pan; bowels moved. Two hours later pulse again rapidly became worse, and the patient died.

This long history is given in detail because of the number of curious facts that may be to some extent explained by the autopsy findings.

Autopsy No. 941. Because of the length of the article the autopsy findings are given in abridged form, with the omission of portions that do not seem to have a direct bearing upon the case.

Body of a poorly nourished adult male. In addition to the usual postmortem lividity there were irregular areas of dark, purplish color over the limbs and trunk, and also on the ears and cheeks. Abdomen considerably distended. Operative incision as previously described. Small amount of brownish, foul-smelling fluid free in the peritoneal cavity. Parietal peritoneum showed glistening surface, except in left hypochondrium, where the diaphragmatic and parietal surface over a region corresponding to the previous location of the spleen was thickly studded with small, raised, grayish-white nodules. The spleen had been removed at operation. The omentum was loosely adherent at the line of incision and around the pedicle of the spleen. Its color was dark and hemorrhagic. Vessels were considerably dilated. No thrombosis found.

Intestines: The intestines were markedly distended and the walls were completely relaxed. Serous surfaces had lost all glistening appearance. Color was dark reddish brown throughout the entire extent. Musculature and mucosa were softened and necrotic. Tissues of mesentery of the same dark color and quite swollen. No signs of obstruction or thrombosis in the vessels in the mesentery. The necrosis involved the entire intestinal tract except the sigmoid and rectum, but it was further advanced along the regions supplied by the superior mesenteric artery. The retroperitoneal glands were slightly enlarged and dark in color.

Stomach: Externally the organ showed a similar dark brownish color, but its musculature was not necrotic. The mucosa at the pyloric and cardiac extremities appeared congested, and showed some ecchymotic spots, while a band of softening about 12 cm. in whidth, with loss of mucosa in small areas, extended completely around the middle of the organ. No thrombosis found in gastric vessels. The organ was considerably dilated, and contained a large amount of brownish, foul-smelling fluid.

Pancreas: The surrounding and interlobular tissues were edematous, and of a dark brown color. The tail bore the structures ligated with the pedicle of the spleen. There was no evidence of hemorrhage nor of thrombosis of these vessels.

Liver: Color was dark reddish, mottled irregularly by lighter yellowish areas. Capsule was thin and smooth, except for some fibrin flakes along the left anterior margin. It measured 25 x 23 x 8 cm. Weight, 2610 gm. On section the consistency was about normal, and the cut surface presented the same yellowish, mottled appearance. A few small whitish-gray nodules resembling tubercles were found.

Kidneys: Except for their dark congested appearance and some clouding of the parenchyma the kidneys appeared normal.

Pericardium: The pericardium contained a slight excess of clear, yellowish fluid. Surface everywhere was smooth and glistening.

Heart: Subpericardial fat was small in amount. The organ appeared somewhat larger than normal. The right ventricle and auricle were distended. The apex of the left ventricle appeared rather fibrous and the color was paler than elsewhere. The right auricle and ventricle contained rather firm postmortem clots. Tricuspid valve admitted three fingers. Leaflets were smooth. The wall of the ventricle was 0.4 cm. thick. The mitral valve admitted two fingers easily. The leaflets appeared normal. The apex was occupied by what appeared from the interior as a large

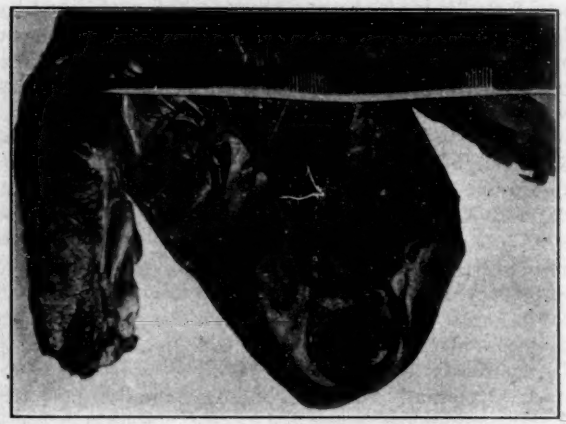

FIG. 1.—Lesions at apex of left ventricle.

mural thrombus, but which on section was evidently a subendocardial process of considerable duration. The muscle was thinned out to about 2 mm. in thickness over it, and internal to this was a dense whitish fibrous stratum about 2 mm. in thickness. Internal to this was a mass of what appeared to be softened thrombus formation. The endocardium from the lateral surface of the cavity appeared to have extended over this mass for a short distance. The diameter of this lesion was about 2.5 cm. At the point of junction of the left posterior and the anterior aortic leaflets was a fresh vegetation, with a narrow pedicle about 3 mm. long. The coronary arteries showed slight thickening and occasional patches of yellow atheroma.

Lungs: Both lungs were considerably congested, but fairly well aërated. Pleural surfaces were normal, except at the right apex

posteriorly, where a few fresh fibrinous adhesions were found. On section the upper lobe showed many conglomerate tubercles toward the central part of the lobe. These showed beginning caseation. A few rather large discreet tubercles were found in the upper right lobe. Apparently the process was a fairly recent one. The bronchial mucosa was slightly inflamed throughout, and a small amount of mucopurulent exudate was present in the larger branches. Bronchial lymph nodes considerably enlarged and showed areas of caseation.

Arteries: At the base the aorta showed numerous areas of well-advanced atheromatous degeneration without calcification or ulceration. The process was marked around the orifices of the

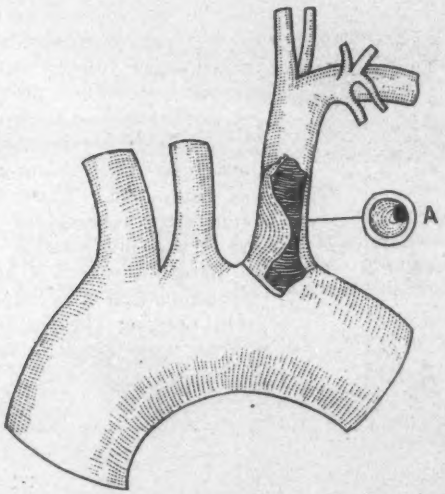

FIG. 2.—Lesion in left subclavian artery. A, Cross section of artery at point indicated.

innominate and left carotid. At the base of the subclavian artery, and extending upward for 1 cm., there was a concentric thickening of the wall, particularly on the inner anterior portion, that narrowed the lumen down to less than 2 mm. The process appeared to have been intramural rather than a canalized thrombus. The descending and thoracic portions of the aorta showed numerous plaques of yellow atheroma without ulceration or calcification, and there was a marked increase in the thickness of the arterial wall in these areas. On the posterior wall of the abdominal aorta there was an ulcerated, calcareous plaque about 1.5 cm. in diameter, to which a firm thrombus was attached. This thrombus extended into the orifice of the superior mesenteric artery, and its upper extremity

was in such a position that it could overlie the orifice of the celiac axis. The renal arteries were unaffected. The atheromatous process was present in the form of scattered plaques well down into the iliac arteries. At the bifurcation there was a firm "straddling" thrombus that extended into the iliacs for about 1 cm.

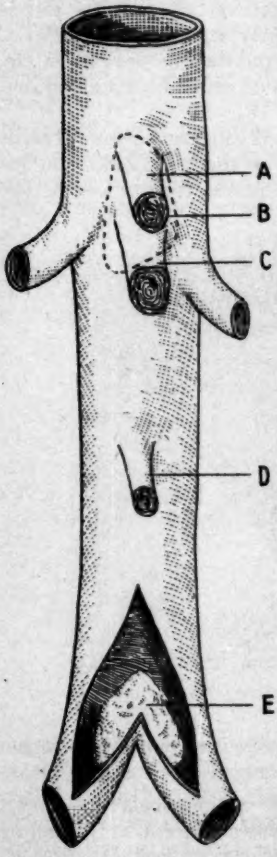

FIG. 3. — Lesions in abdominal aorta; A, obliterated lumen of celiac axis; B, location of thrombus on posterior wall of aorta; C, partial obliteration of lumen of superior mesenteric artery; D, partial obliteration of lumen of inferior mesenteric artery; E, thrombus at bifurcation of aorta.

The superior mesenteric artery was considerably sclerosed at its base, and about 0.7 cm. above this the wall was concentrically thickened so that the lumen was constricted to a diameter of 1 mm. The process appeared to be a fibrosis. Beyond this point the lumen was of normal diameter and the various branches were unobstructed. A similar, but less marked, process was present in the inferior mesenteric artery. At the beginning of the celiac axis the fibrosis was complete, and no lumen was made out. These lesions were found after removal of the organs, and it was not possible to ascertain the nature or extent of any collateral circulation that may have existed.

On opening the femur the bone-marrow was found to be of a dark grayish-red color and of soft consistency.

Anatomical Diagnosis. Gangrene of the intestines with peritonitis; thrombosis of the aorta, superior mesenteric and common iliac arteries; obstructive arteritis of celiac axis, superior and inferior mesenteric and left subclavian arteries; tuberculous peritonitis; pulmonary tuberculosis; tuberculosis of the liver; parenchymatous degeneration of the liver and kidneys; endocarditis, acute vegetative; atheroma of arteries; hyperplasia of bone-marrow. Smears from the lungs and bronchial glands showed a few tubercle bacilli. Material from the lesion in the apex of the heart innoculated into guinea-pigs produced typical tuberculous lesions from which tubercle bacilli were recovered.

REPORT ON THE SPLEEN. Diagnosis: Tuberculosis and Infarction of the Spleen. *Macroscopic Examination:* Specimen consisted

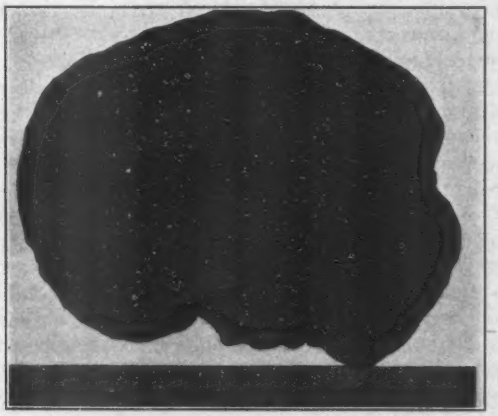

FIG. 4.—Spleen, after hardening.

of a spleen, weight 1350 grams, 22 x 14 x 9 cm. Surface was rough and nodular, with many small (1 to 3 mm.) yellowish areas scattered over the entire spleen. Capsule was thickened, and showed numer-

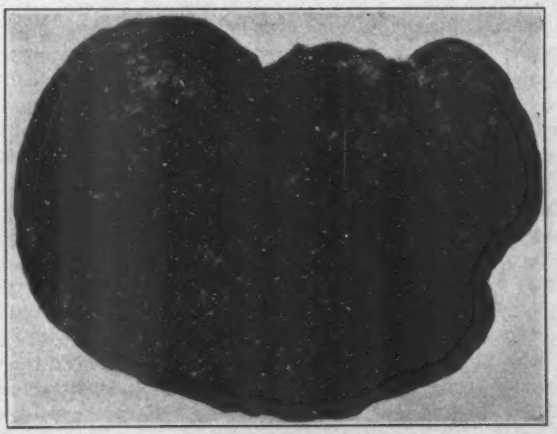

FIG. 5.—Horizontal section of spleen, after hardening, showing areas of tuberculosis and wedge-shaped infarction.

ous adhesions. Opposite hilum is an irregular area 6 x 8 cm. in diameter, much softened, over which the capsule was broken.

Cut surface was red, with innumerable yellowish areas as on the surface; these were firm and fibrous, not caseous. Soft surface area corresponded to triangular infarct extending in 8 cm.; soft fibrous, no yellowish areas. Shades off gradually through hemorrhagic zone into rest of splenic tissue.

Microscopic Examination: Small yellowish areas seen in gross are necrotic tissue, about these were zones of epithelioid proliferation and numerous giant cells of Langhans type. Fibrous tissue of spleen considerably increased. Tissue in infarcted area was entirely necrotic. Small areas of pigmentation were scattered about. No tubercle bacilli were demonstrated in section.

Microscopic Examination. Lungs: The lungs showed marked congestion of the interstitial tissue, and in some areas the alveoli were filled with red blood cells. Small discreet tubercles were numerous; many had coalesced and showed necrosis and caseation. Giant cells were particularly numerous. The smaller bronchi showed slight swelling and desquamation of their epithelium.

Bronchial Glands: Showed typical tubercle formation, with numerous giant cells of the Langhans type. Caseation was only slightly advanced. The proliferation of cells of the epithelioid type was marked. Anthracosis was present in moderate degree. The vessels were congested.

Liver: Showed pronounced congestion and a diffuse degeneration of parenchymatous cells. Many cells of endothelial type were deeply pigmented. Areas showing extravasation of blood and necrosis of the liver cells were numerous. Scattered throughout were numerous tubercles, some of which were undergoing caseation.

Kidneys: There was a moderate degree of cloudy swelling of the tubular epithelium. The glomerular tufts showed congestion and swelling of the epithelium. There was no exudate, and the capsules were not thickened. A few glomeruli were completely fibrosed, and there were a few scattered areas of interstitial fibrosis. The vessels appeared to be of normal thickness.

Diaphragm: The inferior surface in the region of the spleen showed a diffuse tuberculous process. Giant cells were numerous. A few typical tubercles were present.

Heart: Section from lesion in apex of heart showed a slight edema beneath the epicardium and a marked thickening of the walls of the arteries in this region and in the underlying muscularis. There was a slight increase of connective tissue between the muscle fibres, which were also separated by edema. About one-half of the normal thickness of the myocardium was replaced by a firm, almost hyaline fibrous tissue that had a laminated appearance and contained few nuclei. Between the muscle and this fibrous layer was a narrow zone containing many small round cells. Internal to the fibrous zone there was a mass of soft red thrombus with no evidence of organization present. In a few areas small groups

of polynuclear leukocytes were found. In one portion of the wall of the lesion there was an arrangement of the fibrous tissue in whorls that was suggestive of the fibrosis of an old tuberculous area, otherwise there was no evidence that the lesion was due to tuberculosis.

Arteries: Sections through the constricted portion of the superior mesenteric and left subclavian arteries showed a subintimal fibrous tissue hyperplasia that by concentrically thickening the wall of the vessels had markedly encroached on the lumen. In the section from the subclavian artery there was a well-marked round-cell infiltration between the area of fibrosis and the musculature, but there were no giant cells or tubercle formation.

Bone-marrow: Smears from the marrow of the femur showed the usual forms of marrow cells and an abundance of normoblasts. Normal red blood cells composed about one-third of the smear. There was practically no fat present.

A review of the history of this case for the purpose of ascertaining the sequence and possible etiology of lesions gives but little aid. From a clinical standpoint the existence of the marked polycythemia was the most interesting feature of the case. The tuberculous lesion in the spleen would seem to offer a simple explanation for this, and, in fact, attention was called to an enlargement of this organ as early as 1908, although it was not until October, 1910, that a polycythemia was demonstrated. The symptoms of flushing and congestion of the face, which continued intermittently throughout and which may or may not have had a possible cause in the polycythemia, began three years before, in 1905. Moreover, repeated examinations of the heart and lungs from 1905 until the final illness failed to reveal either a circulatory or pulmonary lesion, nor was any other evidence of tuberculosis noted.

Since primary tuberculosis of the spleen is rare, it would be reasonable to expect that some evidence of a more probable primary focus in the lungs would have been manifested. The history of pneumonia with pleurisy in 1902 is suggestive as a possible starting-point for a pulmonary focus, but the autopsy did not seem to indicate a pulmonary lesion of such long standing. However, if one wishes to regard the marked diffuse tuberculosis of the spleen as the cause of the polycythemia, a sufficiently reasonable sequence of events is present on which to base an assumption of such an etiology.

Many of the symptoms referable to disturbance of the digestive tract are readily explained, if it be agreed that the lesions found in the walls of the arteries were of ten years' duration. The various attacks of "indigestion," dizziness, blindness, and the two attacks of hemorrhage could be regarded as caused by an interference with the blood-supply of the digestive organs. In spite of the fact that the second hemorrhage was attributed to high blood-pressure,

and that venesection apparently relieved certain other symptoms, there is no record of a pressure above 140 mm. The vascular lesions must certainly have been of long duration and of a development sufficiently slow to permit of the formation of an extensive collateral circulation. The completeness of the obstruction of the celiac axis and mesenteric arteries permits of no other supposition. The lesions themselves offer little suggestion as to their origin, or to any etiological association with the polycythemia. The lesion in the apex of the left ventricle appeared to be of the same general nature and age as those in the arteries.

Whether the final attack beginning in October, 1912, was precipitated by a lighting up of an old pulmonary tuberculosis, or whether the failing blood-supply to the spleen caused a dissemination of its tubercle bacilli and a starting-point for an acute infectious process, must be left to conjecture. The most obvious cause of death was the gangrene of the intestinal tract, which must be attributed to the lesions found in its arterial supply.

Obviously there is little possibility of any inferences being drawn as to the result of operation in cases of tuberculosis of the spleen or of polycythemia, from our experience in this case. Of course, the autopsy findings demonstrating the obliterative arteritis of the celiac axis and superior mesenteric vessels resulting in gangrene of the intestines and causing death showed plainly the futility of any therapeutic measures in this particular case. And if this arteritis had not caused an early fatal termination, the lesion in the apex of the heart with its thrombus, shown to contain tubercle bacilli by guinea-pig injection, might reasonably be expected to result fatally within a short time.

It is of interest to note that in the present case, during the nine days after splenectomy, the red cell count remained high, between 8,800,000 immediately after operation to 7,400,000 on the day of his death, while the hemoglobin remained at over 120 per cent. This result one would expect if it is true that "the spleen is the graveyard of the red blood corpuscle" in the adult, although Pearce and Austin,[23] in a study of splenectomized animals, found results indicating the power of the lymph glands and liver cells to compensate, after the loss of the spleen, by taking up its function of destroying red corpuscles. However, Musser[24] found "that there was, after experimental splenectomy, a secondary anemia which lasted about two and one-half months." He also found a postoperative leukocytosis most marked twenty-four hours after operation, and lasting a variable time. His counts were continued one hundred and thirty-eight days in some cases, and the leukocytosis was still present. There was a marked increase in the poly-

[23] Jour. Exper. Med., December, 1912, vol. xiv.
[24] Archiv Int. Med., 1912, ix, 599.

nuclear cells, and a diminished lymphocyte count. In the present case this postoperative leukocytosis was a marked feature, reaching 87,000, with 98 per cent. of polynuclear cells on the second day after operation, and then gradually falling, but not back to normal.

It has previously been suggested that the tuberculosis of the spleen, in view of the autopsy findings, might be the simplest explanation for the polycythemia on the basis that the diseased spleen failed to destroy the red corpuscles. Other case reports of polycythemia, however, show numerous examples of the disease in which the spleen while enlarged was not tuberculous, and in twenty-six of the cases of tuberculosis of the spleen where the blood count was reported, collected by Winternitz, polycythemia was present only in six. Also, the condition of the bone-marrow in this and in other cases, and the blood-picture after splenectomy, would seem to indicate as a more logical presumption, that whatever may be its cause, the polycythemia, and in this case it was a polycythemia and not an erythrocythemia alone, had its direct pathological factor in the overproduction or overfunctionating of the bone-marrow. If this presumption is correct, then we can explain the enlargement of the spleen as an hypertrophy due to an effort to destroy the over-production of red cells. Finally, if there is a focus of tuberculosis elsewhere in the body from which the tubercle bacilli might enter the blood-stream, it would find in the spleen a place of diminished resistance. Thus, rather than as an etiological factor, the tuberculous spleen would be a result of the polycythemia.

Finally, while we may agree with Winternitz that in cases of tuberculosis of the spleen, when other tuberculous foci are not demonstrable, splenectomy may effect a cure; although our case proves nothing, it does add some evidence to the statement of Osler that splenectomy is contraindicated in erythrocythemia, and that when the two conditions coexist operative procedure can be of no value.

GIANT TUMORS OF THE CONUS AND CAUDA EQUINA.[1]

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Tumors of the cauda equina and of the conus cause symptoms which are considered fairly pathognomic. Nevertheless, the lesion

[1] Read at the meeting of the American Neurological Association, Washington, May 5, 1913.

is usually, at one time or another, mistaken for some other disease, and, on the other hand, patients are submitted to operation for tumor of the cauda or conus, and some other affection or no gross changes may be found. Then, again, the results of operation for tumor of this region, leaving aside the nature of the tumor, are by no means uniform. It is difficult for a neurologist to say to a patient with symptoms of cauda or conus tumor what will be the certain result of the operation advised. All this makes it imperative that the details of every case encountered should be published.

The tumors that we shall describe, probably originate from the pia over the roots or from the roots of the cauda equina themselves; they grow slowly, causing a few symptoms until they have attained a large size. Finally, when the symptoms are well-marked, the tumors fill the entire lower part of the spinal canal, surrounding the roots of the cauda equina and extending upward upon the conus and lumbosacral cord.

CASE I.—A male, aged forty-two years, Russian Hebrew, married, peddler. Complaints: Difficulty in walking, weakness and stiffness in the lower extremities. Pain in the centre of the small of the back radiating into the hips; inability to have full control of the vesical sphincter; irregular twitching of the right thigh, which always precedes expulsion of urine.

Duration of the symptoms was nine months, and the initial symptom pain, continuous, made worse by standing or walking, and relieved somewhat by lying down. Course of the disease steadily progressive. No history of syphilis.

On close inquiry, after the patient came into the hospital, an interesting story was obtained from him: which was that nine years before, while walking on a railway, he fell and struck his back. He was laid up for a fortnight. About one year afterward, that is, eight years before coming to us, he began to complain of pain in the lumbar region and in the posterior surface of the right thigh. This pain lasted for about eight or nine months, and he went to a hospital in New York City and stayed there for several weeks. Off and on since then he has had some pain in the back and in the thigh. Two years ago he had a severe attack and he justifies himself in stating that the beginning of his present illness was nine months before, by the fact that he was able to work until that time.

Physical Examination. Nutrition: No observable change. Motion: Station feeble, scarcely able to stand securely. Gait: jerky and spastic movement of the right foot in walking, the left normal. Paralysis: Right leg was weaker than the left. Mechanical restriction: No limitation of motion in the lower extremities. Marked rigidity of the lumbar spine. Reflexes: Right knee-jerk absent, left barely elicitable on reinforcement; both ankle-jerks absent; plantar jerks not elicitable; upper abdominals and epigastric reflexes lively; lower abdominals and cremasterics could not

be elicited; upper extremities normal. Disturbances of sensation illustrated by accompanying chart (Fig. 1); laboratory examinations were negative.

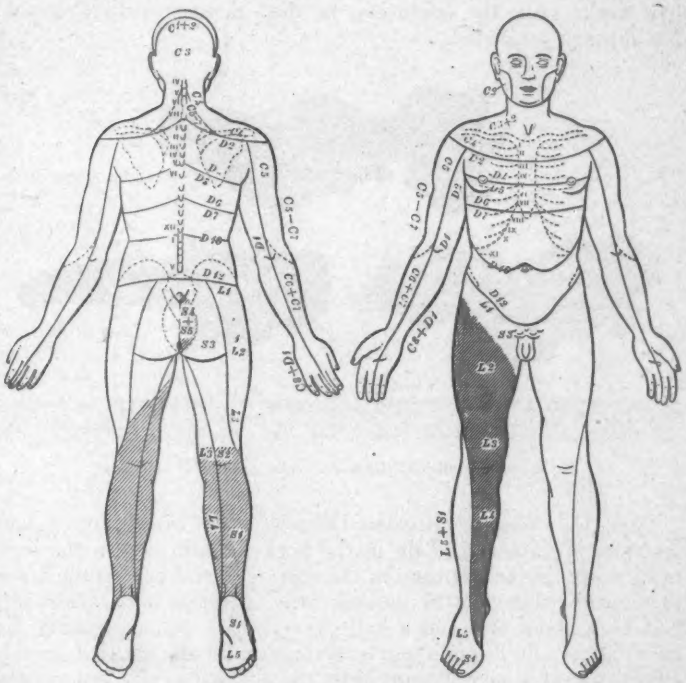

FIG. 1.—Case I. Nathan S., sensory disturbance for touch, pain, and temperature. Close shading, moderate diminution; coarse shading, very slight diminution in sensation.

Surgical History. January 27, 1910: Laminectomy (Dr. Elsberg). The spinous processes and laminæ of the twelfth dorsal and first, second, and third lumbar vertebræ were removed. The exposed dura was of a bluish color on account of a tumor mass beneath it. After incision of the dura a large brownish growth (Fig. 2, I) was exposed, which enveloped the roots of the cauda equina and extended up on the conus. Above the tumor was well encapsulated and could be freed without difficulty; below it was impossible to separate it from several of the nerve roots without dividing them. The growth filled up the lower part of the spinal canal, and below, small fragments of tumor tissue were undoubtedly left behind. Suture of dura, muscles, fascia, and skin.

The tumor measured 2 by 5 cm., and weighed 14 grams; it was soft and not very vascular. It was an endothelial sarcoma. The

patient recovered from the operation, and the wound healed by primary union. After a few weeks he began to look badly, the urine became loaded with albumin, casts, and pus. Four weeks after the operation he was markedly anemic. On February 29, five weeks after the operation, he died in a convulsive attack. No autopsy permitted.

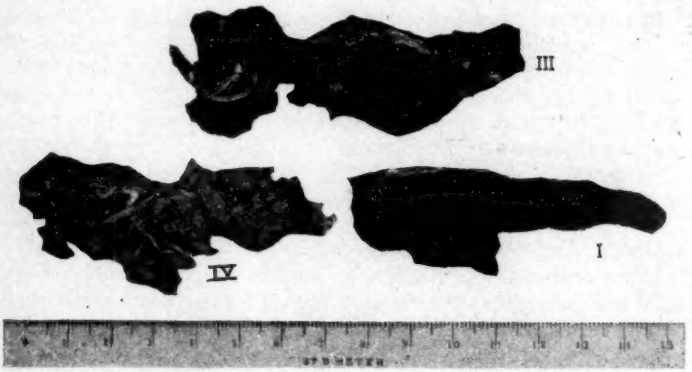

FIG. 2.—Giant tumor of the cauda equina removed at operation.

CASE II.—Woman, Russian Hebrew, aged twenty-five years; married. Complaints: Pain in the back radiating down the legs, more severe in the left than in the right leg; weakness in the lower extremities; difficulty in passing urine. Duration of symptoms had been about two and a half years, initial symptom being the pain. This pain began about a fortnight after she married, gradually increased in severity, and since the birth of a child, ten months after marriage, it had grown worse rapidly. Pain increased by any attempt at movement, such as walking or going up and down stairs, and was least when lying down.

She had been subjected to many kinds of treatment. Had worn arches for double flat-foot; had been in a plaster jacket for alleged spinal trouble, etc.

Physical Examination. Nutrition: Nothing noteworthy save a faint systolic murmur at the apex, hemic in character. Station: Weak and uncertain. Gait: Shuffling, "rooster" gait. Paralysis: Drop-foot on both sides. Marked stiffness of the lumbar spine. Reflexes: Knee-jerks faintly elicitable; ankle-jerks present; plantar flexion; abdominal and epigastric reflexes present. Sensation: As indicated on the chart (Fig. 3).

It is noteworthy that percussion on top of the head caused intense pain in the lumbar spine, and that the lumbar vertebræ themselves were tender on percussion.

Laboratory examinations were all negative, save that the lumbar puncture brought forth a dark yellow fluid which contained no cells, gave a negative Wassermann, and coagulated solid on application of heat.

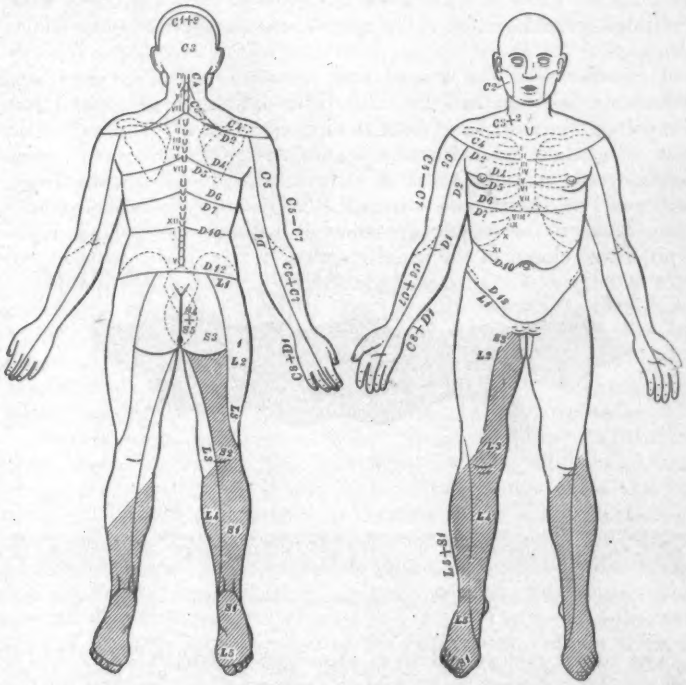

FIG. 3.—Case II. Mrs. P., very slight disturbance of touch, pain, and temperature over shaded areas.

Surgical History. December 3, 1910: Laminectomy (Dr. Elsberg). Removal of spinous processes and laminæ of the third, fourth, and fifth lumbar vertebræ, later of the second and first lumbar and the twelfth and eleventh dorsal vertebræ. The exposed dura was of a bluish color, and did not pulsate. There was evidently a large neoplasm within the dural sac. The dura was incised, exposing a large reddish-brown tumor mass, which surrounded the roots of the cauda equina and filled up the entire spinal canal to the lowermost part exposed. Above it was necessary to remove the eleventh and twelfth dorsal and first and second lumbar arches, and to incise the dura upward, before the upper end of the tumor was exposed. The growth extended upward upon the conus and lumbosacral cord, and was well-limited and but slightly adherent

to the cord. During the various manipulations the tumor gradually bulged out of the canal until it seemed about three times as thick as when first exposed. Below could be seen some roots of the cauda equina surrounded by tumor tissue. It was deemed advisable to delay the removal of the growth in order to allow the tumor to be extruded from the canal. The wound was therefore closed without drainage.

December 10. The wound was reopened and the tumor was found markedly extruded. With little difficulty the growth was freed from the conus and from the inner surface of the dura, which was everywhere smooth and glistening. The growth was likewise easily freed from the roots of the cauda, although it was firmly adherent to the filum terminale. Several fragments of tumor tissue had to be separately removed with a sharp spoon. The wound was closed in the usual manner.

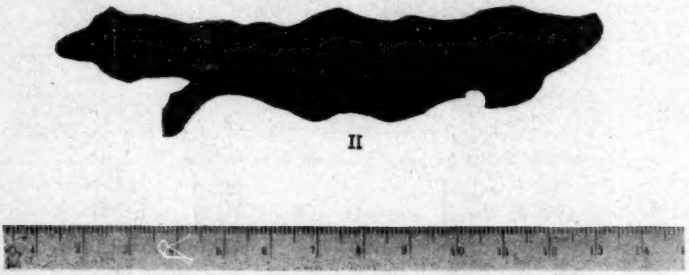

FIG. 4.—Giant tumor of the cauda equina and conus removed from Mrs. P.

The tumor removed (Fig. 4) measured 14 cm. in length and 6 cm. in circumference in its widest part, and was reported by the pathologist as endothelial sarcoma. Convalescence from operation uncomplicated.

December 17. Slight flexion and extension at the knees was possible.

January 6, 1911. Power in the right lower extremity was better than in the left, flexion at thigh and hip—about 75 per cent. of the normal on the right, about 30 per cent. of the normal on the left.

January 20: Discharged from the hospital. Patient had gained much flesh and strength; could stand on her feet when aided; was able to extend and flex both legs with ease; knee- and ankle-jerks were still absent.

September 6: Patient continued to gain flesh and strength. Could walk, but had trouble on account of the persistent foot-drop. Knee- and ankle-jerks were still absent. Patient was free from pain; no disturbance of sensation could be found.

CASE III.—Male, Russian Hebrew, aged thirty years, married, painter. Complaints: Pain starting in the middle of the small of the back and extending down both thighs and legs; weakness of the lower extremities so that walking was difficult; inability to pass urine; impotence.

The initial symptom was pain in the middle of the back, which was not continuous in the beginning. It was made worse by exercise, and was relieved by hot applications and a hot bath. His first incapacity was in bending over and in straightening up after he bent over. After the pain had existed in one lower extremity for about three months it appeared in the other. At this time he was seen by a number of neurologists and was treated as a case of sciatica. His symptoms had been in existence for about two years when we first saw him. Course of symptoms had been steadily progressive.

Physical Examination. Nutrition: The skin of the feet was soft and shiny, the nails strikingly convex, with transverse markings. Motion: When the feet were lifted from the ground there was distinct drop-foot on both sides. Gait: Typical "rooster" gait. Station: He stood fairly securely when his feet were together when the eyes were open, but swayed when the eyes were closed.

There was no muscular atrophy. Reflexes: knee- and ankle-jerks absent. Plantar reflex was flexor in type; abdominal and epigastric reflexes were lively; cremasteric reflexes could not be elicited. There was a diminished response to the faradic current in the peroneal muscles, more marked on the right side. There was distinct stiffness in the lumbar vertebral column, and the lower lumbar spines were sensitive to pressure and percussion. The sensory disturbances are indicated in Fig. 5. There was a distinct area of exquisite hyperesthesia at the upper border of the sacrum. On doing a lumbar puncture, the needle, after entering the cavity, gave the operator's hand a sensation of there being some friable substance encountered, and the patient complained of a burning sensation transmitted down the right hip and leg. No fluid was obtained.

Surgical History. October 4, 1911. Laminectomy (Dr. Elsberg). Removal of the spines and laminæ of the first, second, third, and fourth lumbar vertebræ and later of the eleventh and twelfth dorsal. Shining through the dura, which was very thin, was a reddish-brown tumor mass, over which were spread the roots of the cauda. Incision of the dura revealed a large tumor, which filled the spinal canal from the sacrum below to the conus above. The actual removal of the growth was left to a later stage, so as to allow of the extrusion of the growth.

The tumor was removed one week later; above, it was well limited and easily freed from the conus; below it surrounded the roots of the cauda and not all of the tumor could be removed. In spite of

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careful dissection, small fragments of tumor tissue had to be left behind. Bleeding was moderate; closure of the wound in the usual manner.

The tumor was 10 cm. long (Fig. 2, III), and was reported as being an endothelioma.

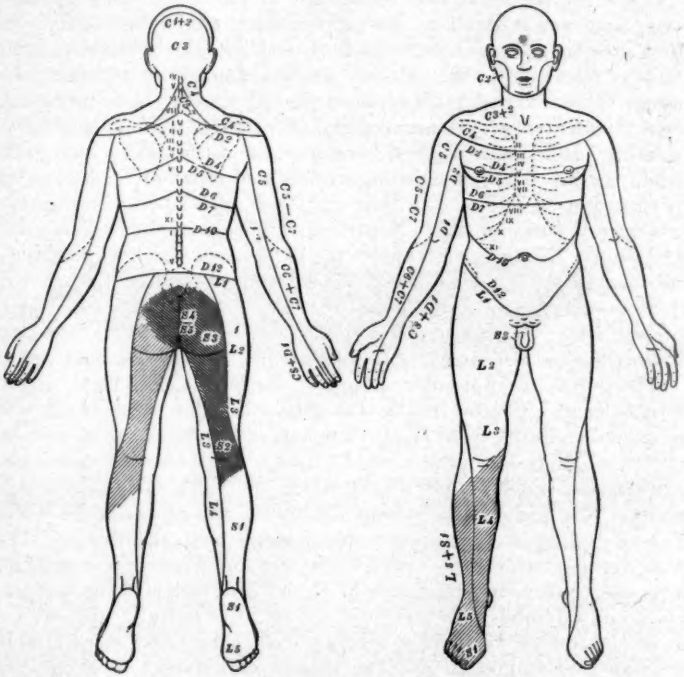

FIG. 5.—Case III. J. S., sensory disturbances for touch, pain, and temperature. (Shading the same as in Case. I.)

Convalescence was uneventful. Two weeks after the operation the patient was able to urinate voluntarily, and the pain in his back and limbs was somewhat less. He was discharged from the hospital three weeks after the operation. Two months later, sexual power had returned, but the patient complained much of a stiff feeling in his legs and of frequency of urination.

March 1, Patient had been receiving injections of Coley's fluid and *x*-ray treatment twice each week. Still complained of stiffness in his legs and frequency of urination; knee- and ankle-jerks were still absent. No longer had foot-drop; sensory disturbance unchanged.

January 22, 1912. The patient was last examined on this date. His complaints were: Pain in the back and right thigh; feeling of stiffness; obstinate constipation; no feeling when his bowels moved; weakness of the legs; incontinence of urine.

He stood securely, with his back not stiff, walked with a stick, with a slightly shuffling gait. The tendon-jerks of the lower extremities were absent, and the only striking difference from his condition before the operation was in the objective sensory disturbance and the disappearances of the foot-drop.

Each of these three patients presented a clinical picture and physical signs so similar to the others that a diagnosis of the similar nature of the disease could be made. In Case I the diagnosis was suspected; in the two succeeding patients the diagnosis of giant tumor of the cauda equina endothelioma or endothelial sarcoma was made before the operative interference.[2]

The important features of the clinical histories in our patients were the following:

1. A history of two or more years' duration.
2. Pain in the small of the back, sooner or later extending down one and then the other extremity.
3. Stiffness of the back in the lumbar region.
4. Increasing stiffness and weakness of the lower extremities, with loss of power of dorsal flexion of the foot.
5. Slight disturbances of the bladder and rectum.
6. The patients were treated for sciatica for long periods.

The important features of the clinical examination were the following:

1. Rigidity of the lumbar vertebral column.
2. Weakness and stiffness of the lower limbs.
3. Paralysis of the peroneal groups of muscles and sometimes of the tibialis anticus group.
4. Drop-foot on one or both sides.
5. Absence of knee- and ankle-jerks.
6. Tenderness of the lower lumbar spines.
7. Irregular and unsymmetrical sensory disturbances.
8. Lumbar puncture was negative, or yellow fluid which was not cerebrospinal fluid was withdrawn.
9. Wassermann test and *x*-ray negative.

The typical findings at operation consisted of a large reddish-brown, not vascular, tumor within the dura, which filled up the entire lower part of the spinal canal, surrounded the roots of the cauda equina, and extended upward on to the conus, with which it was not closely connected. The growth was not intimately connected with the inner surface of the dura, and could be easily freed

[2] One of us has operated upon two additional patients. One patient was on the service of Dr. Bailey at the Neurological Institute, the other was a private patient referred by Dr. W. M. Leaynsky, of New York.

from it, after which the inner surface of the dura mater was found to be smooth and glistening. The growths were well encapsulated above, but were closely connected with the nerve roots below.

The typical history and findings in these patients were similar to the so-called syndrome of epiconus lesions described by Minor of Moscow, which may be outlined as follows: The patient begins to complain of pain and stiffness in the back, extending down the posterior aspect of one and then of the other thigh. The pain is intermittent at first, later it is continuous. After the expiration of one year or more the symptoms become worse, one or double drop-foot appears, the lower limbs become weaker and stiffer, and knee- and ankle-jerks disappear. Then follow difficulties in the functions of the bladder and rectum, irregular sensory loss, rigidity of the lumbar vertebral column, and tenderness of the lumbar spines. Peroneal palsies are regularly found, with electrical changes. By lumbar puncture no fluid is obtained, because the entire lower part of the spinal canal is filled by the tumor mass, although yellow fluid in small quantity may be withdrawn from the tumor. The patients are often suspected of tabes, and usually have been treated for long periods for sciatica.

PECULIAR FEATURES OF THE TUMORS, AND REMARKS. We are fully cognizant of the fact that, in a general way, the symptoms and signs we have outlined are those generally described as characteristic of lesions of the cauda equina and conus. But they have been combined in a peculiarly characteristic manner in our cases.

The late appearance of bladder and rectal disturbances in the patients lends support to the view of Spiller[3] and of van Gehuchten as against that of Müller[4] that bladder and rectal symptoms need not appear early in intradural pressure upon the roots of the cauda equina.

Another peculiar feature in these patients was the relatively small evidence of sensory disturbances. According to some authors (Laquer, Kummel Schmoll), sensory symptoms, in lesions of the cauda equina and conus, may be absent for years. Müller claims that in the lower end of the cord the sensory roots are larger than the motor roots, but he agrees with Klineberger that the sensory elements have a marked resisting power. It is difficult to understand why there is not a greater sensory loss in these patients, with large tumors which fill up the entire lower part of the spinal canal. The typical anesthesia in the perineum, genitals, and around the anus was usually incomplete, ill-marked, or absent. This was the more surprising as at operation the tumor was usually found to surround the roots of the cauda—those centrally situated as well as those on the outside. That these large tumors were under con-

[3] AMER. JOUR. MED. SCI., 1908, xxxv, 368.
[4] Deutsch. Zeit. f. Nervenheilkunde, 1899, xiv

siderable pressure was proved by the fact that as soon as the dura was opened they bulged markedly out of the canal.

The tumors were relatively benign in their course, they had no tendency to perforate the dura or to invade the surrounding bony structures. In this respect they differed from many of the cases of diffuse intradural sarcoma in the literature (Schultze,[5] Spiller,[6] etc.) and were like those reported by Selberg[7], Warrington,[8] Klineberger,[9] etc.

The results of the operative interference were not satisfactory, although there was considerable improvement in two of our patients. It was impossible to remove the growths entirely, although most of it could be removed if the operation be divided into two stages so that the tumor be allowed to extrude from the spinal canal in the manner described. In the one patient who received injections of Coley's fluid and *x*-ray treatment, not much was gained thereby. While the danger from the operative interference was small, our only hope for radical removal lay in our ability to recognize the existence of the tumor early and to refer the patient to the surgeon early. If the patients had been operated upon before the tumors had attained such large size, radical removal might have been possible.

SOME CASES OF HYPOTENSION ASSOCIATED WITH A DEFINITE SYMPTOMATOLOGY.

By Edward H. Goodman, M.D.,

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It is difficult to state just how low the systolic pressure may fall and yet be considered normal. In an individual who has been observed over a period of time and in whom one has determined a uniform pressure, any deviation from this standard may with justification be regarded as abnormal if not pathological. But for the rank and file of individuals it must remain a purely arbitrary judgment at what figure to place the lower limit of normal pressure, and the standard thus erected must be regarded as but an individual opinion, nothing more.

Janeway draws the line between normal and subnormal systolic pressure at 100 mm. Hg. (R.R. 5 cm.) and 90 mm. (12 cm., G.).

[5] Mittheil. a. d. Grenzgebieten, 1903.
[7] Beiträge z. klin. Chir., 1904, xliii, 197.
[9] Monatsschr. f. Psych. u. Neurol., 1908.
[6] Amer. Jour. Med. Sci., 1908, cxxxv.
[8] Lancet, 1905, ii, 749.

I prefer using the auscultatory method, to place the limit at 120 mm. Hg., and I believe pressures below this must fall in the category of lowered or low blood pressure. Such a limit is purely empirical, and observations made with a standard instrument, with a uniform method, and under uniform conditions, in many thousands of healthy individuals, this procedure alone can fix the limit with any degree of accuracy.

The maintenance of blood pressure depends primarily on the preservation of the normal peripheral resistance and on the force of the cardiac systole. The following lines copied, in the main, verbatim from Cannon[1] gives a concise view of conditions which tend by decreasing peripheral resistance, to cause lowered blood pressure.

"Fall of pressure is seen in poisoning by chloral and alcohol, both of which paralyze the vasoconstrictor centre. The collapse of the circulation that sometimes occurs in the course of certain of the infectious diseases, such as pneumonia and diptheria, may be in part due to this cause. In surgical shock, again, the widespread abolition of vascular tone is accomplished by a low blood pressure. In these instances the reduction may be due to a rapid pouring of the blood out of the relaxed vessels or to a stagnation of the blood in the veins to such an extent that the heart does not receive a sufficient supply to continue its normal discharge. Which of these conditions plays the more important role is not yet determined. Henderson has argued from evidence which he has accumulated that the condition of shock[2] is attributable entirely to a failure of the supply of venous blood to the heart.

"As is well known, vasoconstrictor tone can be diminished at will by use of the nitrites. A few whiffs of amyl nitrite produce a sharp drop in arterial pressure, which is, however, soon regained.

"A physiological condition attended by lowered arterial pressure is sleep.

"A low pressure may be due not to vasodilatation but to a weak heart, and any agency used to increase vasoconstrictor tone under these circumstances is likely to stop the heart at once. Indeed, my attention," says Cannon, "has recently been called to a case of precisely this character in which the administration of adrenalin to raise the pressure was followed by instant death—the laboring heart was overburdened by the sudden increase of load and stopped immediately. Until the part played by each of the two factors, therefore, the heart and the arterioles, is clearly discriminated the intelligent treatment of any disturbance of normal arterial pressure is impossible."

[1] Boston Med. and Surg. Jour., 1911, clxv, 672. [2] Amer. Jour. Phys., 1910, xxvii, 158.

The causes of hypotension or the condition in which hypotension is a phenonenon may be classed as follows:

1. Acute infections, excepting epidemic cerebrospinal meningitis.
2. Chronic wasting diseases: carcinoma, tuberculosis, cachexia from whatever cause, Addison's disease.
3. Hemorrhage, drugs, chloroform.
4. Nervous diseases: general paralysis of the insane neurasthenia, after epileptic seizures, sometimes in tabetic crises, after lumbar puncture, Basedow's disease (at times), osteoarthritis, exhaustion, shock—surgical or anaphylactic.
5. Cardiovascular diseases: tachycardia, dilatation of the heart, arteriosclerosis (at times), mitral stenosis, decompensatory cardiac lesions.
6. Blood dyscrasias: anemia, polycythemia cum sphenomegaly.
7. Renal condition: cyclic albuminuria, nephritis (at times) amyloid disease.
8. Intoxications: alcohol, tobacco, acute adrenal insufficiency.
9. Terminal hypotension preceding death.

A search of the literature reveals a lamentable paucity of specific articles on low blood pressure, the subject of hypertension apparently having dominated the interest and riveted the attention of writers. Anyone who includes blood-pressure estimations in the routine examination of every patient must have been impressed, however, with the not infrequent occurrence of blood pressures below 120 mm. Hg., blood pressures lying between 110 and 120 mm. Hg. Less common are the pressures lying between 100 and 110 mm., and still more rare are those between 80 and 100 mm.; but apart from exciting surprise at the abnormally low tension the phenomenon seems to have been little investigated. It is on account of the very cavalier treatment of the subject, that contributions devoted to its explanation or papers dedicated to report of cases are extremely valuable. If one reads all references to hypertension he will be astonished at the amount of research performed along these lines, and will gather the incorrect and hasty impression that hypertension is the only problem in sphygmomanometry. It cannot be denied that a persistent high blood pressure carries in its train more destruction and more pernicious damage, and that therefore it deserves more consideration than does low pressure; yet this seems hardly a satisfactory explanation on for the neglect which hypotension has experienced.

Its importance and significance in certain surgical conditions, notably shock; in certain clinical crises, such as anaphylactic shock; and its almost constant presence in acute fevers or infections; these are well-established facts. They are valuable additions to our knowledge, no doubt, but hypotension in cases other than in the above, in individuals who present no apparent lesion but who con-

sult the physician about symptoms to which the specious diagnosis neurasthenia might be too readily applied, hypotension in these patients is a subject well worth the study. Whether the low blood pressure in certain persons is a cause of the symptoms or whether it is a result of some agent causing the symptoms one cannot say.

The subject of hypotension has made a special appeal to Münzer,[3] who presents his paper with three prefactory remarks, with the censure that the subject has received but scant attention, with the expressed aim to separate certain cases into groups, and with the frank admission "wobei ich mir dessen (einige Formen) wohl bewusst bin, dass es bei dem gegenwärtigen Stand unseres Wissens nicht möglich ist, das Gebiet systematisch zu erschöpfen." Münzer endeavors to classify his cases in groups, and succeeds in forming six. Some of his arguments for this grouping and the basis for his diagnosis seem to be dogmatic rather than irrefutably sound. His paper, nevertheless, has this value, that it frankly invites criticism, its avowed object being to stimulate interest in the subject of hypotension.

The first of Münzer's groups is the hypotension seen in arteriosclerosis. He believes that this is a common cause of low pressure, and offers as explanation that the blood flows through the large hard vessels, as does a fluid through an unyielding tube; there being no periodic distention of the vessel wall, the tension is lowered. In some instances the pressure was as low as 85 systolic, 75 diastolic. A common trilogy of symptoms was headache, vertigo, and even fainting.

A second group of cases occurs in what Münzer believes to be status thymo lymphaticus. Wiesel[4] and later Hedinger[5] observed hypoplasia of the chromaffin system in cases of this kind, and since Schur and Wiesel[6] have demonstrated hypertrophy of the chromaffin system in cases of hypertension, Münzer believes one may, by analogy, expect hypoplasia to be associated with low blood pressure. He proceeds on insufficient grounds, I believe, to arrange certain cases in the category of status thymo lymphaticus.

The remaining groups of disease associated with hypotension are orthostatic albuminuria, chronic nephritis, paroxysmal tachycardia, and cachectic conditions.

That hypotension is by no means an uncommon feature of arteriosclerosis there can be little doubt, as Huchard's reference in the *Transactions of the XVI International Medical Congress*, in Budapest (1909), will show: I have under my care at the University Hospital Medical Dispensary a case in point.

[3] Wien. klin. Woch., 1910, p. 1341.
[4] Virchow's Archiv, 1904, Band clxxvi.
[5] Ztsch. f. Pathol., 1907, p. 527.
[6] Deutsch. med. Woch., 1907, No. 51.

Thomas MacR., aged sixty-seven years, engineer, was referred from the eye dispensary with retinal hemorrhages in the left eye. There was decided arteriosclerosis and urinary findings suggesting intestitial nephritis, *i. e.*, polyuria, low specific gravity, albumin, and casts. The blood pressure, which in this case was a variable quantity, had been as low as 123 to 80 mm. Hg.

I have been most interested in cases of low blood pressure occurring in the absence of any demonstrable organic lesion. These have been patients, for the greater part, on the ascent or the crest of the curve of life, who have presented certain symptoms common to each, and who have been markedly improved by practically the same therapeutic measures. As illustrative cases, the following are quoted. (Auscultatory method; Stanton sphygmomanometer; Widecuff.)

CASE I.—H. F., female, aged twenty-three years, consulted me July 14, 1911, on account of headache. Patient had been complaining of headaches for the previous two or three years. The attacks were intermittent, there being often two or three months' interval, and then again repeated several times in the same week. The headaches were situated in the top of the head and were described as pulsating and throbbing in character, with a feeling of tenseness. The patient could ascribe no cause for the headaches, although sleep usually brought relief. She had less endurance than formerly, and "played out" readily. Bowels were regular, no gastric symptoms. Eyes were thoroughly refracted five years before.

The family history and previous medical history were negative. The menses were regular, but the patient had some pain in the right iliac region, from which she suffered a good deal at irregular intervals. There was no aggravation of headache at these times nor at the time of menstruation.

The physical examination was negative. The blood pressure at the time of the first visit was 80–55 mm. Hg. Under treatment during the next four months the blood pressure rose to 120 mm. Hg., and with this improvement the headaches disappeared almost entirely.

CASE II.—E. C. W., female, aged thirty years. Referred by Dr. Langdon. On the evening of September 25, 1911, I was summoned to give relief for a severe headache. The patient stated that since the spring of 1911 she had suffered intensely with violent frontal headache, vertigo, swelling of eyes and of ankles, scanty urine, and less endurance. In August, 1911, she underwent a severe nervous strain, and admitted in September that she was at the "end of her rope."

Patient says she has at times of periods pain over the right ovary, and that her menstruations are irregular. Owing to the fact that

her mother experienced the menopause when thirty-five years and her maternal grandmother had "change of life" at thirty-two years, patient is apprehensive and fearful that her present symptoms may be phenomena incidental to what seems to be a familial early menopause. Bowels regular.

On examination the urine was found to be negative. The blood: Hemoglobin, 80 per cent.; erythrocytes, 4,030,000; blood pressure 110–75. Large doses of bromides brought about amelioration from the headaches, and the patient was sent to the country for a three weeks' stay. On her return she stated that in this time she had had four severe attacks. Blood pressure, 115–65; hemoglobin, 90 per cent.

In December, at which time the blood pressure had risen to 120–70, the patient stated that she had not felt so well for years, and that she had not had a headache for over a month.

February 28, 1912, patient came to see me on account of slight return of headaches during the previous week. Blood pressure, 110–60 mm. Hg.

March 20, 1912, with a rise in pressure, there was subjective improvement, and apart from a feeling of distention after meals the patient felt "first-rate."

CASE III.—F. J. G., male, aged fifty-one years, lawyer. Referred by Dr. E. I. Keffer, November 28, 1911. His chief complaint was failing of memory. Patient had been for thirty years of a nervous disposition, and had received sporadic treatment during this time for his trouble. Lately he had found his memory to be less keen in court work; he was so fearful of himself in public that he was beginning to devote himself entirely to office consultations. With the failing memory he had had persistent insomnia, and was subject to unaccountable attacks of irritability. He complained of no headache, but described his mental symptoms as if a cloud were enveloping his brain. Vertigo persistent, but not severe, was an unpleasant symptom. He "played out" both mentally and physically; would get up tired in the morning, and had difficulty in concentrating his attention. He was insistent that he had not worked hard for five years, but his law partner adduced evidence to the contrary.

The patient had some gastric symptoms, flatulence, belching, and acid eructations. Appetite was variable, but ate everything. Bowels were regular. Apart from overindulgence in tobacco there was nothing in the patient's further history which seemed to have a bearing on the case.

On examination his lungs were negative; heart was enlarged, slightly to the left; there was a systolic murmur at the apex transmitted slightly. After removal of a test meal (125 c.c., total acid 74, free HCl 32) the stomach was found to be slightly dilated,

lower border 2 cm. below umbilicus. The liver was slightly palpable. Blood: hemoglobin, 90 per cent. Urine and feces negative; blood pressure, 105–55. Eyes were refracted five years before.

Treatment seemed to be ineffective with this patient, that is, blood pressure rose to 116, but could be brought no higher. The patient had persisted, however, with the suggestions made to him and at the last visit, September 23, 1912, stated that he saw a marked improvement since a year before, and that for the last two weeks he had felt better than ever before. Blood pressure at that time was 123–55. He had regained his confidence when talking in public and had lost his fear of being unable to express himself in the courts.

CASE IV.—R. E. G., male, aged twenty-one years, statistician. Referred by Dr. Knowles Feb. 15, 1913. Chief complaint, constipation and eruption on the face. Dizziness from "some cause or other."

The acne he had had for five years, but constipation made its appearance five or six weeks before. The previous summer he began to have dizzy spells, which were gradual in onset. These attacks followed exercise or any mental stimulus. Although he does not faint, he seats himself as quickly as he can, as he thinks he might fall if he stood. There is no nausea or vomiting. He feels perfectly well as soon as the dizziness passes off, which it does in a few minutes. He has no headaches. Eyes were examined October, 1912.

Patient takes a good deal of exercise in the form of walking, although he studies, as a rule, about ten hours a day. No gastric symptoms. He is losing weight; best weight 130 pounds, three years ago; now 117 pounds.

Patient's habits are exemplary. The family history discloses a nervous taint in all members of the family.

Examination is negative. Blood pressure, 110–60.

March 22, 1913. No more dizziness. Bowels regular; weight 121½ pounds; blood pressure, 120–60; feels fine.

CASE V.—G. L., male, aged forty-two years, laborer. Admitted to my dispensary at the University Hospital January 20, 1913, complaining of intermittent spells of dizziness.

Patient states that these spells come on once every week or two. Each attack was preceded by a feeling of warmth, then his sight was blurred. There was numbness in the head, followed by vertigo. Patient reels if standing, and has to support himself to avoid falling. "Spells" only come on while standing. If patient lies down the spell passes off in about an hour, but if he remains standing they may last half a day. As he recovers, he is nauseated, has a gnawing pain in the epigastrium, and sometimes vomits.

He is unable to talk "much." No symptoms remain after the spell. He is constipated, and takes laxatives several nights a week; otherwise the gastrointestinal tract is negative.

During the attacks he has a bearing-down sensation of the brows and double vision. He notices sensation of constriction in fauces and pharynx. Mouth floods with saliva, and at the same time he experiences difficulty in swallowing. This is followed by a feeling of nausea, and at times he may vomit. He also feels an epigastric pulsation. He has difficulty in breathing, his head feels too heavy for his body, and he dreads falling from dizziness, therefore keeps his eyes on the ground during attacks. He has no noises in ears. Had eyes refracted about a year ago and lenses corrected. Hypermetropic astignatism, but this has in no way influenced his attacks, which come with some degree of periodicity once every week. Has some slight palpitation of heart on exertion; marked hypotension.

These five serve as illustrations of certain phenomena associated with hypotension. Although not each symptom is present in every instance, the chief symptoms in these cases are headache, vertigo, mental and physical tire. These symptoms have been significant, inasmuch as one or all have been the chief complaint of the patient, and with rise in pressure the patients have been much improved. The question which naturally arises is, What is the etiological factor?, and to this there must be a confession of ignorance. Tuberculosis must be the condition to suspect whenever there is a lowered blood pressure, provided no other cause such as tabulated above can be found, but in none of these five patients whose histories have been reproduced was there slightest evidence of this infection. It would be purely supposititious to hold that a small lesion might still be present and escape careful physical examination. There is no clinical evidence to support this hypothesis, and improvement followed a course of treatment which would presumably have had a somewhat opposite effect in tuberculosis.

Can the low pressure be an expression of auto-intoxication? Inasmuch as this theme has been so well worn that we perceive the insubstantial warp, one should omit it from his medical diagnosticum. The more closely one studies the cases of supposed auto-intoxication the more frequently does he find an underlying organic condition to explain the symptoms, such as hepatic cirrhosis, enteritis, redundant sigmoid, visceroptosis, etc. If one is to take the symptomatology as given by Combe ("Auto-intoxication intestinale") as an indication of an underlying intestinal intoxication, he will be able to ascribe to the latter practically every symptom flesh is heir to. There may be *bona fide* cases of auto-intoxication, but these must be very few. At any rate the methods at our disposal for their recognition are at fault, and an estimate formed from quantitative and qualitative urinary examinations, no matter how

painstaking and exact, is by no means a correct one. Feeling that auto-intoxication is a poor diagnostic term I prefer not to consider it as a cause or as the cause of the symptoms exhibited by these patients.

Were constipation a common feature in these cases it might be assumed that retention of feces with absorption of waste products—in other words, auto-intoxication again—might be the cause of the hypotension. Correction of the constipation then might bring about amelioration of symptoms. In only one case was constipation a feature, and as no drugs were given for this, reliance being placed on certain exercises, the problem is not so simple. It is a question, moreover, whether constipation alone is associated with absorption of certain waste products. I am by no means convinced that it is. Again, it is a nice point to decide whether constipation is the cause of the hypotension or whether the hypotension, with its other symptoms of tire, might not bring about relaxation of the intestinal musculature as it does of the voluntary muscles. And may it not be true that with increased vasomotor tone, normal action of the intestines has been brought about, rather than that relief from constipation has raised the blood pressure by eliminating the absorption of waste products?

The diagnosis of neurasthenia applies here as little as does that of auto-intoxication. Neurasthenia seems to be a convenient diagnostic catch-all for conditions not perfectly understood, and great care should be executed in making this diagnosis. Moreover the blood pressure is not lowered in neurasthenic states, but raised, as shown by Stursberg[7] and Stursberg and Schmidt.[8]

I confess that I can offer no explanation of the hypotension. The significant features in these cases is that subjectively they were alike, and with the same method of treatment all showed improvement and some were cured, and with this improvement as cause or effect, was associated an increase of blood pressure.

TREATMENT. The treatment which has been given these patients consists essentially of the following: They are instructed to go to bed at a reasonable hour and to rise at a certain time each morning. Immediately on rising they are to perform a series of exercises, consisting of free movements, somewhat after the following plan:

1. Stand erect with the arms extended and the fingers in contact above the head. Stoop forward and try to touch the floor with the finger-tips, moving slowly, and return again to the original position.

2. Lie at full length on the floor or bed upon the back, with the

[7] Deutsch. Archiv. f. klin. Med., 1907, xc, 548.
[8] Münch. med. Woch., 1913, p. 174.

hands under the hips, and bring each leg alternately and slowly to a position at right angles to the body. Perform the same motions with both legs conjointly.

3. Lying at full length upon the back, the hands clasped behind the head, bring the elbows in, bend the body forward until the face touches the knees, returning again slowly to the original position.

4. Standing position: extend the arms sidewise, the elbows straight, until the hands meet above the head. Stretch the arms as much as possible in doing this. Inhale deeply as the arms go up, and exhale slowly as they come down.

5. With the hands on the hips, the thumbs behind, without moving the feet, turn the trunk as far as possible to the right, then to the left. As the body turns rub the fingers deeply into the abdomen.

6. Raise the arms laterally, the palms upward, until the level of the shoulders is reached, bring them forward until the fingers touch; then reverse the movement, extending the arms backward as far as possible, at the same time rising upon the toes.

7. Breathing: Hands at hips, head backward bend, inhale through nose; head erect, exhale through nose and mouth five to ten times.

In order that the exercises should have the desired effect, they must be performed regularly, every morning, at least ten minutes being devoted to the task. They should at first be performed slowly, with intermissions of a few seconds for rest and deep breathing. As the muscles become accustomed to the work they may be increased in rapidity and duration, but never to the extent of producing exhaustion or prolonged breathlessness.

Following these or some such exercises, a shower-bath, first hot and then as cold as can be well borne, should be taken, but if there are no such appointments, a good modification can be obtained from the following:

Stand erect in the tub in which a little hot water remains, and sponge the entire body quickly with cold fresh or salt water; or pour a pitcher of cold water over the back and spine, or use a douche or spray. This should be immediately followed by a brisk rub with a coarse towel, continued long enough to produce redness of the skin. Following this, rest in the recumbent position, well covered up, for five or ten minutes before dressing. Bath-room should be warm.

Definite rules are given for the number of hours work to be done a day, and a certain amount of relaxation is insisted upon. Golf, horseback-riding, tennis, walks in the country, are all useful in bringing about a temporary dropping of business, professional, or domestic trials.

In all of these cases I have prescribed ascending doses of tincture

of nux vomica, beginning with 15 drops three times a day after meals and increasing 3 drops a day, so that the first day, 15 drops three times a day are taken, then 16, 17, and so on. The limit to the increase is the first sign of the physiologic action of the drug, and when this is obtained the dose is dropped 5 drops and maintained there for a period of two to five days, after which the number of drops is decreased 15 drops a day, dropping from 45, for example, 40, three times a day, to 35, three times a day, etc. The decrease is continued to the original 15 drops three times a day, which dose is maintained for a week, and then the nux vomica is discontinued.

Regarding the dose of nux vomica which may be given, patient Case III took 75 drops three times a day without experiencing any physiologic effect of the drug. The individual tolerance to strychnine is variable, and not everyone can take such large doses without feeling some toxic effect.

For the coexisting constipation use was made in the following manner of the exercises described by Fernet.[9] I quote from my article in *Progressive Medicine*, December, 1912, p. 102.

"The patient, before arising in the morning, is to lie on the back, and take five or six deep breaths, with the mouth closed, protruding and retracting the abdomen with each respiration. After a few moments of natural breathing the same procedure is repeated, and is kept up for five or six times. By means of the deep breaths, Fernet claims that the abdominal organs are subjected to a kind of massage, which is further augmented by manual massage during the remissions of normal breathing. After rising and bathing the patient should partake slowly of breakfast, and afterward go to the toilet, whether he feels the desire to defecate or not. If there is no bowel movement the breathing exercises should be repeated, and in place of the massage, rectal gymnastics should be practised, consisting of voluntary movements of the anus, efforts of expulsion and of retension. Under no condition should there be any straining."

Excessive indulgence in tobacco, alcohol, tea, and coffee when confessed to should be corrected. These and other detrimental habits, too individual to enumerate, should receive due attention, the object being, by means of a sensible conduct of life, to bring the bodily functions to a normal state of activity.

Edgecombe[10] writes that his attention has been attracted to a class of cases, suffering from no disease in particular, but complaining of general slackness and want of tone, with a systolic pressure frequently below 100 mm. Hg. (Oliver). He records

[9] Bull. de l'Acad. de Méd., 1911, 3d series, lxv, 662.
[10] Practitioner, 1911, lxxxvi, 515.

night and morning readings of systolic pressure in a subject for two hundred consecutive days, and his observations are of great interest. After trying all sorts of remedies in this case, he says the permanent raising of a low pressure is a matter of great difficulty. He has found that a small rise is coincident with marked amelioration, and regards exercise, diet, and change of residence to high altitudes preferable to drug treatment. His subject was a large meat-eater, and he recommends elimination of this staple from the dietary.

To his statement that it is difficult to raise a lowered blood pressure there can be no opposition, and I am also in accord with him when he says small rises in pressure bring about marked improvement of the condition. I am inclined to believe that of all the measures to employ in raising blood pressure in such cases the least to be considered are drugs, although I should be unwilling to abandon the use of strychnine when given in full doses as described above.

THE CLINICAL SIGNIFICANCE OF DIASTOLIC AND PULSE PRESSURE.[1]

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In the last few years the importance and clinical value of determining blood pressure has become recognized and the procedure now stands among the indispensible methods employed in physical diagnosis.

The more recent graduates and certainly all up-to-date clinicians now make frequent observations of the systolic blood pressure; but comparatively few estimate diastolic pressures, and of this number many fail to understand the significance of their observations.

The reason for this is inability to appreciate the significance of or to intrepret the diastolic readings is clear.

Until the use of the auscultation method of determining blood pressure was introduced by Karokow in 1905, it was virtually impossible to obtain accurate and uniform diastolic readings outside of a clinical laboratory, where large cumbersome recording instruments were used, so that the wide differences in diastolic readings obtained by different men made any accurate scientific

[1] Read before the Jefferson Hospital Clinical Society, November 21, 1913.

observations impossible. As a consequence, most observers became discouraged and considered diastolic blood pressure readings of no clinical value. Further, there has up to the present time been comparatively little work done on diastolic pressure, so that the clinician has but few observations from which to draw conclusions. Since the advent of the auscultation method, however, it has become a comparatively simple matter to obtain accurate diastolic readings.

The main question now at issue is what constitutes the *true* diastolic pressure when the auscultation method is employed. Is the diastolic pressure represented by the height of the mercury column when the second thumping sound becomes dull or when all sound disappears? For example, after one has applied the cuff of the blood pressure apparatus to the patient's arm and inflated it until all pulsation below the cuff is obliterated, then by releasing the air pressure slowly and listening with the ordinary binaural stethoscope over the line of the artery below the line of the cuff one hears a loud clear thump when the arterial wave first passes the constricting cuff. The height of the mercury column read at this moment indicates accurately the systolic pressure. If one continue to listen over the artery and to release slowly the air pressure, the first thumping sound is replaced by a murmur, which in turn, is followed by a second thumping sound which gradually becomes louder, then fainter, and shortly thereafter disappears. The question under discussion is whether the true diastolic pressure is represented by the height of the mercury column at the time the second thumping sound is loudest or when all sound is gone. At the present writing it has been clearly shown, especially well by the work of Dr. Louis N. Warfield,[2] that the true accurate diastolic reading should be made at the time the second thumping sound is loudest. It is, however, much easier in most cases to determine the time of disappearance of all sound, which gives a reading approximately 3 to 5 mm. lower. For clinical purposes the disappearance of all sound will suffice, with the exception of cases of aortic regurgitation, in children, in patients with widely dilated arteries, and in high pressure cases where the difference may amount to 8 to 16 mm. of mercury.[3]

Thus, the determination of diastolic pressures is as easy by auscultation as the making of systolic readings. The auscultation method is the only accurate one by which the general practitioner can determine diastolic pressure.

The sooner clinicians realize that it is impossible to obtain accurate diastolic readings by determining the lowest point of the maximum oscillation of the mercury column or the aneroid needle,

[2] Interstate Med. Jour., October, 1912.
[3] Louis N. Warfield. Jour. Amer. Med. Assoc., October 4, 1913.

and use only the auscultation method, the sooner will we be in a position to obtain a series of accurate diastolic pressures which will be invaluable.

Up to the present time I have been speaking of diastolic pressure readings applicable to adults and older children and have only alluded to infants. In these and small children the auscultation method of obtaining blood-pressure readings is not applicable, as the arteries are so small that the sounds are not distinguishable, and in many cases not audible.

In this class of cases the pith ball indicator first utilized by Fedde[4] as a diastolic indicator has its place.

The indicator as devised by Fedde afforded no means of determining systolic pressure and, unfortunately, owing to its mechanical arrangement, will not give accurate diastolic readings in infants, though it was applicable to adults.

Later Raymond B. Hoobler[5] modified this apparatus by using a double cuff and stopcock connection between them in circuit with the pith ball indicator. By this new and ingenious device both diastolic and systolic pressures could be recorded, even in infants.

After considerable work with this apparatus, finding some difficulty in making the readings conform to those obtained by the auscultation method, I changed the mechanical construction of the pith ball indicator so that now the readings correspond exactly with the observations obtained by the auscultation method, where the two methods can be utilized on the same patient.

Before going further it might be well to understand exactly what is meant by diastolic and pulse pressures.

Just as the systolic pressure is an indicator of the force of the ventricular contraction of the heart, so is the diastolic pressure, the pressure existant when the heart and vessels are at rest, an indicator of the amount of peripheral resistance present in the arterial system.

By subtracting the diastolic from the systolic pressure we obtain the pulse pressure, which in turn represents the head of flow. In other words, it represents the excess force the heart exerts over and above the peripheral resistance represented by the diastolic pressure. It is the amount of pressure which carries on the circulation.

The importance of diastolic and pulse pressure at once becomes apparent when it is understood that the first represents the amount of resistance the heart has to overcome to cause the blood to flow, and that the second shows how much excess of pressure the heart is exerting to carry on the circulation.

While the systolic pressure by itself may furnish a great deal of information, it may also be misleading unless checked up with

[4] Medical Record, July 16, 1910.

[5] Ibid., December 30, 1911.

the diastolic and pulse pressure. As an illustration: Given a man aged sixty years; on taking his systolic pressure it is found to be 135 mm. Hg.; you naturally conclude that he is a well-preserved man, unless you estimate his diastolic pressure, which, we will say, is found to be 110 mm. Hg. Then the whole picture is changed, you know that the systolic pressure has been much higher, but that the heart muscle has become degenerated, and can no longer maintain the high systolic pressure it should, so that you have the small pulse pressure of 25 mm. Hg. The peripheral resistance indicated by the diastolic pressure of 110 mm. Hg. is high, but the heart cannot maintain a relatively high systolic pressure, so that the pulse pressure is only 25 mm. Hg., instead of about 47 mm. Hg., as it should be, with the diastolic pressure of 110 mm. Hg.

The pulse pressure where the auscultation method is used to obtain the systolic and diastolic pressures should be approximately 35 per cent. of the systolic pressure. In ordinary ranges the pulse pressure is from 25 to 40 mm. Hg. .

Recently there has appeared an article by Willard J. Stone[6] in which he emphasizes the importance of determining the pulse pressure and uses the formula of the pulse pressure divided by the diastolic pressure as indicating the cardiac load. He gives the normal pulse pressure as 50 per cent. of the diastolic pressure, and states that in the severer cases of myocarditis, with failing compensation, the pulse pressure is often greater than the diastolic pressure, which by his formula gives the cardiac load as over 100 per cent. This is a new presentation of the subject of diastolic pressure, and merits extended study and trial.

As more attention is paid to maintaining the normal pulse pressure clinicians will be less ready to administer nitrites to every case of hypertension, as though simply lowering systolic blood pressure would cure them. Much serious injury to many patients will be avoided by observing the fact that as long as in an advanced case there is a normal pulse pressure for a corresponding diastolic reading only harm will come from the use of vasodilators, which lower the systolic pressure and thereby lessen the blood flowing to the various organs of the body.

Often it is simply a question of placing the patient under the best hygienic conditions and maintaining the pulse pressure at about the normal for the corresponding systolic reading. In fact, in advanced arterial conditions, where there are actual arterial changes in the vessel walls the patient's condition is often best treated by the administration of small doses of digitalis and strychnine for their tonic effect on the cardiac muscle and the avoidance of all vasodilators. Since a patient's life should be regulated in accordance with the diastolic and pulse pressures and therapeutics directed to the general cardiac condition.

[6] Jour. Amer. Med. Assoc., October 4, 1913.

By noting the diastolic pressure and determining the pulse pressure unnecessary stimulation, which would only wear the heart out, can be avoided.

Frequently there is a condition of low systolic pressure due in no respect to cardiac weakness, but to the fact that the arteries and capillaries are widely dilated, as indicated by a low diastolic pressure, the pulse pressure being within a normal range. In these cases, which are often found during the convalescence from a severe illness as pneumonia, influenza, etc., cardiac stimulation is often resorted to because the average practitioner, feeling a small pulse wave or it may be finding the systolic pressure low, immediately concludes the heart is failing and stimulation is required. Nothing could be more erroneous and the stimulation which is not needed simply whips up a heart to beat against a lessened resistance, and the effect produced is similar to that when an automobile engine is allowed to race with all the power on, by releasing the clutch.

In pneumonia one of the most valuable aids in the diagnosis, prognosis, and treatment is the proper determination and interpretation of the diastolic and pulse pressure together with the systolic pressure. The diastolic pressure will often tell whether there is vasomotor dilatation, in which case it will be low, or whether there is a marked venous stasis, in which event the pressure will be high. In the one case vasoconstrictors are called for, while in the other vasodilators or possible venesection is the proper treatment.

Between the pulse rate and the diastolic pressure there is a very intimate relation, well described by Sir Lauder Brunton.[7]

If the pulse is slow more time is allowed for the blood to flow through the arterial system during diastole, and the diastolic pressure is lowered and the pulse pressure increased.

In a weak heart the tension is not raised as rapidly as in a strong one, the pulse is rapid and the time between systoles is shorter and the pulse pressure lower.

In a strong heart the pulse is slower and the intervals between systoles is longer and there is a larger pulse pressure.

When the arterioles contract a high diastolic pressure and a small pulse pressure result, and *vice versa*.

Given a low systolic pressure with a large pulse pressure you probably have a strong heart with dilated vessels.

A low systolic pressure with a small pulse pressure indicates that the heart itself is weak, being unable to maintain the normal pulse pressure. In this case there is usually some dilatation of the vessels, too.

If there is a high systolic pressure and a correspondingly high

[7] British Med. Jour., November 5, 1910.

diastolic pressure we may assume that there is a normal balance between vessels and heart and that a compensatory condition is present. In all probability there is either an acute or chronic toxic condition, where the high pressure is temporary and will return to normal as soon as the cause is removed, as overeating, etc., or there are arterial, nephritic, and cardiac changes of a permanent character, which not being removable as the damage is already done, can best be treated by conserving the general nutrition of the patient and preventing the development of further changes.

The question is one of balance, it being important to know not so much the pressure the blood is under as the volume of fresh blood delivered to the organs. The actual figures representing the systolic blood pressure may be an aid but they are not important in themselves.

It is essential, in addition, to determine the pulse pressure, as the velocity of flow of the blood stream is roughly equal to the pulse pressure multiplied by the pulse rate. While there are other factors and this is not absolutely accurate in every case, it gives a very good idea of the amount of blood supplied to an organ.

I wish to emphasize the importance of taking the systolic, diastolic, and pulse pressures in every case and impress upon you the ease and accuracy with which this may be attained by the auscultation method.

In taking diastolic readings a great deal depends on the instrument used as well as the method employed.

Three essential qualities of a practical sphygmomanometer have become prominent: (1) Accuracy; (2) portability; (3) durability.

Up to the present time no sphygmomanometer has fulfilled all these requirements.

Some of the mercury instruments have had accuracy and durability, but have lacked portability.

The aneroids, on the other hand, have been portable, but the statements of such prominent physicians as Dr. Richard C. Cabot, Dr. Oscar H. Rogers, chief medical director of the New York Life Insurance Company, and himself the inventor of an aneroid, Dr. J. W. Fischer, Chief Medical Director of the Northwestern Life Insurance Company, Dr. George Oliver, of London, and too many others to mention, have plainly shown the shortcomings of aneroids in point of accuracy and durability.

Realizing the importance of accuracy, portability, and durability, I have devised a new pocket mercurial sphygmomanometer, which I believe embodies all three features named.

It consists of a metal case, which encloses and protects all the glass portions. This makes it durable and eliminates frailty. The lid, when raised, automatically locks in the upright position, and acts as a support for the instrument.

Fig. 1 shows the instrument just after the lid is raised. On the

lid is securely mounted by metal clips a cylindrical reservoir (G), partly filled with mercury, into the top of which projects the tortuous tube (F). The top of the reservoir is connected by a union to the metal piece containing the needle-valve (C), the metal connection (B) and the stop-cock (A). The bottom of the reservoir is connected by a U-bend with the glass tube (K), which ends in the steel stop-cock and is fastened to the lid by the metal clamps (I and L). Alongside and parallel to the tube (K) is a folded metal scale (J) which hinges in the middle. At the edge of the lid alongside the glass reservoir is the metal tube (E) containing the glass tube (H) with its ground end.

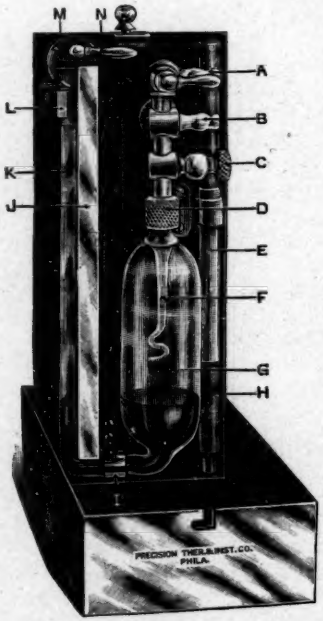

FIG. 1.

To operate, the handle (N) of the stop-cock (M) is raised, the glass tube (H) is removed from its holder, and the ground end inserted through the open stop-cock (M) into the upper end of the tube (K) which is ground to fit it. The scale is then opened by rasing the lower end upward. After it is opened the scale is adjusted so that the zero is at the level of the mercury in the tube (K).

FIG. 2. shows how the unions (A′ and B′) are inserted into the stop-cock (A) and the connection (B) respectively. One should

make sure that the needle-valve is closed and the stop-cock (A) is open as shown in the illustration.

The soft pneumatic cuff is snugly applied to the patient's arm, and the systolic, diastolic, and pulse pressures are accurately obtained by the auscultation method.

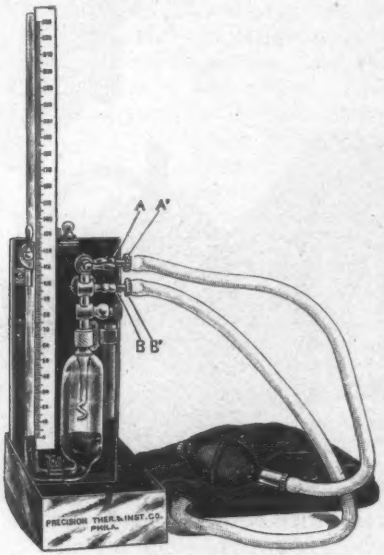

FIG. 2.

One great advantage of this new pocket sphygmomanometer is that by the auscultation method (Fig. 3) the simplest and at the same time the most accurate method of obtaining the blood pressure and the one used by the majority of careful observers, the diastolic pressure is as easily and accurately obtained as the systolic pressure. Also being a mercurial instrument, it is more accurate and dependable than an aneroid, which up to the present is the only other type of instrument that is of equal portability.

The inertia of mercury mentioned as preventing the taking of accurate diastolic readings, has absolutely no significance when the auscultation method is used.

To close the instrument the tube (H) is removed and slid into the metal holder (E). The scale is folded down and then the unions (A′ and B′) removed. The lid will then be found to close by firm pressure on the upper end. As the instrument is shut the handle of the stop-cock projects beyond the end of the case. This

is so arranged to ensure closure of the stop-cock, to prevent any loss of mercury.

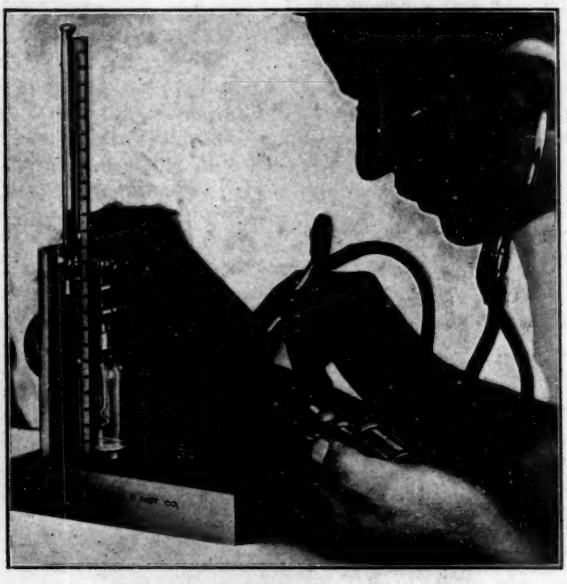

FIG. 3.—The auscultation method.

The instrument fits, when shut, into a morocco carrying-case, the cuff and inflating apparatus alongside it, and after the case is fastened it will slip into the pocket (Fig. 4).

FIG. 4.

ACCURACY. This, the first essential, is obtained in this apparatus by means of the following features: (1) A metal millimeter

scale is used, especially compensated for any lowering of the level in the mercury reservoir. (2) The zero point on the scale is adjustable to the mercury level, so that readings are not affected by climate and temperature. (3) The scale reads directly in millimeters, and being in a vertical line, may be read much more easily than when markings are condensed and on a circular dial. (4) As it is read directly in millimeters of mercury, the primary standard, it does not have to be checked up; one is always sure of the readings; there are no diaphrams to weaken, and there is no delicately balanced needle, actuated by a hair spring. (5) The use of a steel stop-cock and flint glass gives no opportunity for formation of amalgam with the mercury, so there is no black deposit. (6) Redistilled mercury is used. (7) The air release is perfectly even.

PORTABILITY. The entire instrument with inflating apparatus and cuff fit in a morocco carrying-case which slips into the pocket, securing ease of portability. The instrument is so light that it can be readily carried in the coat pocket or in the hand-bag.

DURABILITY. All parts are thoroughly protected by a metal case and are not easily broken or deranged. By a special stop-cock no mercury can be lost. The additional stop-cock (A) is an extra safeguard should the rubber washer in the pump leak a little. Until the washer is replaced the mercury can be maintained absolutely by closing the stop-cock. This is the only pocket sphygmomanometer with this special stop-cock.

In addition the apparatus is simple to operate, it makes use of an accurate, wide, soft cuff which is easily and quickly attached to the instrument by a ground slip joint. An automatic catch on the lid holds the instrument in the upright position when in operation. The mercury remains clean owing to a filter being used, which prevents the powder from the rubber parts being sucked into the mercury reservoir.

This new pocket sphygmomanometer is portable, yet possesses all the accuracy and dependability of the mercury column and is essentially a bedside instrument on which diastolic and pulse pressures can be easily and accurately taken.

THE INHIBITORY ACTION OF CERTAIN ANILIN DYES UPON BACTERIAL DEVELOPMENT.

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Assisted by

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of Houston, Texas.

SECOND COMMUNICATION.[1]

In a recent communication[2] we showed that the inhibitory action which certain violet dyes, like gentian violet, methyl violet, Hoffmann's violet, and others, exercise upon certain bacteria is intimately dependent upon the triphenyl methane structure of these dyes and upon the presence of the three amino groups which are found in all the inhibitory representatives of this class. We have also pointed out that the replacement of the basic by acid auxochromic groups or a diminution of the basicity of the respective compounds by the additional introduction of acid groups leads to a loss of this inhibitory power.

In view of the practical as well as theoretical aspects of this problem, it seemed of interest to us to extend our studies to other groups of dyes also, and it is the purpose of this second paper to present the results of these investigations.

Dyes Investigated. Our studies include representatives of the diphenyl amines (that is, of the indamins and indophenols, the oxazins and oxazons, the thiazins and thiazons, and the azins) of the acridins, of the azo dyes, of the hydrazons, of the azobenzidins, of the thiazols, and the oxyquinones.

The general technique was the same as that described in our first communication, the various dyes being used in the concentration of 1 in 100,000 of nutrient agar. The list includes the following representatives, and has been arranged in accordance with their structural composition and their basicity or acidity, the presence of acid or basic groups in addition to the predominating types being represented by arrows pointing in the direction of acidity or basicity respectively.

The organisms examined were for the most part the same as those which had been used in our investigations of the triphenyl methanes.

Diphenyl Amines.

A. Indamins and Indophenols.

Basic.	Acid.
Phenylene blue	
Bindschedler's green	

[1] Received for publication May, 1913.

[2] Amer. Jour. Med. Sci., vol. cxlvii, No. 2, p. 247.

B. Aurantia.

Aurantia

C. Oxazins and Oxazons.

Capri blue ←—— Gallocyanin
Muscarin ——→
Nile blue
New methylene blue
Coelestin blue ——→

D. Thiazins and Thiazons.

Thionin ←—— Thiocarmin
Methylene blue
Ethylene blue
Toluidin blue
Methylene green ——→
Methylene violet
Methylene azure

E. Azins.

Eurhodins and eurhodoles: — Indulin R.
  Neutral red — Indulin B.
  Neutral violet
Safranins and safranoles:
  Phenosafranin
  Tolusafranin
  Tannin heliotrope
  Amethyst violet
  Echt neutral violet
  Paraphenylene blue
  Indasin
Indulins and indones:
  Naphtazin blue — Naphtazin blue (sulphonic acid derivative)
Aposafranins:
  Neutral blue — Rosindulin G.
  Basel blue

Azo Dyes.

Anilin yellow ←—— Methyl orange
Chrysoidin — Orange G.
Vesuvin — Ponceau
Indolin blue — Roccellin
  Alizarin yellow
  ←—— Citronin
  Dianil red
  Dianil blue
  ←—— Dianil black
  Tartrazin

Azobenzidins.

  ←—— Benzopurpurin
  ←—— Diamin violet
  ←—— Diamin blue
  ←—— Diamin green
  ←—— Pyramin orange
  ←—— Congo red

Thiazols.

Primulin

Quinolins and Acridins.

Acridin orange ←—— Acid quinolin yellow

Oxyquinones.

  Alizarin red W. S.
  Acid alizarin blue

The results which have been obtained with these various dyes in the case of the different organisms that have been examined will be found grouped together in the accompanying tables, the acid dyes being italicized.

Triamino-triphenyl methanes.

		Fuchsin.	New fuchsin.	*Acid fuchsin.*	Methyl violet.	Crystal violet.	Hofmann's violet.	Benzyl violet.	Dahlia.	*Roth violet 5RS.*	Iodine green.	Methyl green.	Ethyl green.	*Acid violet.*	*Eich green.*
St. aureus	1	0	0	++++	0	0	0	0	0	+++	++++	± to +	+	++++	++++
	96	+++	0 to ++	++++	−	0	0	0 to +	0	−	++++	++	++	++++	++++
	40	+++	0	++++	−	0	0	0	±	+++	++++	+++	+	++++	++++
	95	+++	+++	++++	0	0	0	0 to ±	0	+++	++++	+++	++	++++	++++
	42	0	0	++++	0	0	0	0	0	+++	++++	+++	+++	++++	++++
	83	+++	+++	++++	0	0	0	±	0	+++	++++	+++	+	++++	++++
	53	+++	+++	++++	0	+	0	0	0	+++	++++	+++	++	++++	++++
	84	+++	0	++++	0	±	0	0	0	+++	++++	+++	0	++++	++++
	58	−	−	−	0	0	0	−	0	+++	+++	± to +	−	+++	+++
St. pyogenes	2	0	−	−	0	−	−	−	0	−	−	0 to ±	−	−	−
	92	+++	+	+++	0	++	++	0	+++	+++	+++	+++	0	+++	+++
	26	0	−	−	0	0	−	−	0	−	−	+	−	−	..
	93	−	−	+++	+	−	−	−	−	+++	−	−	−	−	−
	28	0	−	−	±	0	−	−	0	−	−	−	−	−	−
	82	−	+++	+++	−	−	−	0	−	+++	−	++	0	−	−
	43	0	−	−	0	0	−	−	0	−	−	0	−	−	−
	85	0	0	++++	0	0	0	0	0	+++	++++	0	0	++++	++++
	50	0	0	++++	0	0	0	0	0	+++	++++	+++	0	++++	++++
	81	+	+++	++++	0	0	−	0	+++	+++	++++	0	0	++++	++++
	54	+++	0	+++	0	++	+	0	+++	+++	++++	+++	0	++++	++++
	57	0	−	−	0	−	0	−	0	+++	++	++	−	−	−
	77	+++	+++	+++	+++	0	+++	0	+++	+++	+++	+++	0	−	++++
	61	0	−	−	0	0	0	−	0	+++	+++	0	−	+++	++++
	78	−	..	−	0	0	+++	−	0	+++	..	0	−	+++	++++
	16	+++	+++	+++	+++	+++	−	+++	+++	+++	+++	+++	+++	+++	++++
	37	0	0	+++	0	0	0	0	0	+++	+++	+	0	+++	++++
	47	−	−	−	0	−	−	..	0	+++	−	0	−	−	−
St. citreus	44	0	0	+++	0	0	0	± to +	0	+++	+	0	+	+++	+++
M. catarrhalis	6	..	..	..	..	..	..	..	..	..	..	..	..	..	..
	100	+++	0	+++	−	−	0	±	0	+++	+++	± to +	+	+++	+++
	41	0	−	−	0	0	0	−	0	+++	+++	0	0	+++	+++
	75	−	−	−	0	0	−	−	−	−	−	−	−	−	−
M. aurantiacus	9	0	0	+++	0	++	0	±	0	+++	+++	++	+	+++	+++
Anthrax	14	0 to ±	0	+++	0	0	0	0	0	+++	+++	+++	0	+++	+++
Actinomyces	15	0 to ±	0	+++	0	0	0	0	0	+++	+++	++	0	+++	+++
Pneumococcus	102	0	−	+++	0	0	−	−	0	−	−	−	0	++	−
	64	±	−	−	+	+	0	−	±	−	+++	+++	−	+++	+++
	29	±	−	−	0	0	−	−	0	−	−	+	−	−	−
Meningococcus	71	−	−	−	0	0	−	−	−	+++	+++	++	−	−	+++
	105	+++	−	−	+++	+++	+++	+++	+++	−	−	−	−	−	−
B. typhosus	3	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
B. paratyphosus	11	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
B. paratyphosus	12	+++	+++	+++	+++	+++	++	+++	+++	++	+++	+++	+++	+++	+++
B. paracoli	19	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
B. coli	32	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
B. enteritidis	8	+++	+++	+++	0	0	0	−	0	+++	+++	+++	+++	+++	+++
B. dysenteriæ	67	+++	+++	+++	+++	++	+++	+++	++	+++	+++	+++	++	+++	+++
	90	+++	+++	+++	+++	+++	+++	+++	+++	−	+++	+++	++	+++	+++
	68	+++	+++	+++	+++	++	+++	+++	++	+	+++	+++	++	+++	+++
	69	+++	+++	+++	+++	++	+++	+++	+++	+++	+++	+++	+	+++	+++
B. pyocyaneus	70	++	+++	+++	+++	++	+++	+++	++	+	++	+++	++	+++	+++
	7	+++	−	−	+++	+++	++	−	+++	+++	+++	+++	−	++	+++
B. subtilis	4	0	−	−	0	0	0	−	0	+++	+++	0	−	+++	+++
	13	+++	−	−	0	0	−	0	0	+++	+++	+++	−	+++	−
V. choleræ	20	+++	..	..	+++	..	..	+++	..	..	..	+++			

METHANES. DIPHENYL METHANES.

Oxytriphenyl methanes.		Phthaleins.				Pyronins.						Diaminotriphenyl methanes.				
Aurin.	*Corallin.*	*Fluorescein.*	*Uranin.*	*Eosin.*	*Erythrosin.*	6 G.	Rhodamin. 3 B	Rosazein, 6 G.	Rosazein, B.	*Sulphorosazein, B.*	Pyronin.	Malachite green, FFO.	Brilliant green.	*Acid green.*	G.	Auramin. OO.

. QUINOLINS AND ACRIDINS.

				Indamins.		Aurantia.	Oxazins and Oxazons.								
		Quinolin yellow.	Acridin orange.	Phenylene blue.	Bindscheidler's green.	*Aurantia.*	Capri blue.	Muscarin.	Nile blue.	New methylene blue, GGN.	*Gallocyanin.*	Coelestin blue.	Ultracyanin.	Thionin.	Methylene blue.
St. aureus	1	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
	40	+++	+++	..	..	+++	++	+++	+++	0 to ±	+++	+++	+++	+++	+++
	96	+++	+++	+++	++	+++	+++	+++	+++	+	+++	+++	+++	+++	++
	42	+++	+++	..	..	+++	± to +	+++	+++	+++	+++	+++	+++	+++	+++
	95	+++	+++	..	..	+++	+++	+++	+++	0	+++	+++	+++	+++	++
	53	+++	+++	..	..	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
	83	+++	+++	..	..	+++	+	+++	+++	+++	+++	+++	+++	+++	++
	84	+++	+++	..	..	+++	++	+++	+++	0	+++	+++	+++	+++	+
St. pyogenes	82	+++	+++	..	..	+++	−	−	−	2 0	−	0	−	−	−
		..	..	..	..	..	..	..	..	26 0	..	..	..	..	..
	92	+++	+++	..	..	+++	++	+	++	92 0	+++	0	+++	+++	++
	93	−	−	..	..	++	+++	−	+	−	−	−	−	−	−
	50	+++	+++	+++	0	+++	0	+++	+	+++	+++	0	+++	+++	++
	85	+++	+++	..	..	+++	0	−	0	0	+++	0	+++	+++	0
	54	+++	+++	..	..	+++	0	+++	+++	0	+++	0	+++	0	0
	81	+++	+++	..	..	+++	0	+	0	+	+++	0	+++	+++	0
	57	−	−	..	..	−	−	+++	+	0	−	−	−	0	−
	77	−	+++	..	..	+++	0	−	+++	−	+++	0	+++	+++	−
	61	−	−	..	..	−	−	+++	0 to ±	0	+++	−	−	−	0
	78	−	−	..	..	−	+++	−	++	−	+++	−	+++	−	−
	16	+++	+++	+++	0	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
	32	+++	+++	+++	0	+++	+++	+++	+	+++	+++	0	+++	+++	+++
St. citreus	44	+++	+++	..	..	+++	++	+++	++	0	+++	+	+++	+++	0
M. aurantiacus	9	+++	+++	..	..	+++	+++	++	+	+	+++	+++	+++	+++	+++
M. catarrhalis	6	+++	+++	..	..	+++	+	+++	++	0	+++	+++	+++	+++	+++
	100	+++	+++	+++	0	+++	±	+++	++	0	+++	+	+++	+++	++
	75	−	−	..	..	++	0	−	−	−	−	−	+++	−	−
	41	−	−	..	..	++	0	+++	0	0	+++	−	++	−	−
Pneumococcus	102	−	−	..	..	−	−	+	−	−	−	0	−	−	+
	64	−	−	..	..	−	−	+++	+++	0	+	−	−	−	−
Meningococcus	71	−	−	..	..	−	−	+++	+	−	+++	−	−	−	−
	105	−	−	..	..	..	..	..	..	+++	..	..	..	..	±
Anthrax	14	+++	+++	+++	+	+++	± to +	+++	+++	++	+++	0 to ±	+++	0 to ++	0 to +
							0 to +++								
Actinomyces	15	..	..	..	..	..	0 to +++	+++	..	..	+++	0 to ±	..	0 to ±	0 to ++
B. typhosus —α	3	+++	+++	..	..	+++	+++	+++	+	+++	+++	0 to +++	+++	+++	++
B. paratyphosus —β	11	+++	+++	..	..	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
B. paracoli	12	+++	+++	..	..	+++	+++	+++	+++	+++	+++	+++	+++	0	+++
B. coli	19	+++	+++	..	..	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
B. dysenteriæ	32	+++	+++	..	..	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
	67	+++	+++	..	..	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
	90	+++	+++	..	..	+++	+++	+++	+++	−	−	+++	+++	+++	+++
	68	+++	+++	..	..	+++	+++	+++	+++	+++	+	+++	+++	+++	+++
	69	+++	+++	..	..	+++	+++	+++	+++	++	+++	+++	+++	+++	+++
	70	+++	+++	..	..	+++	+++	+++	+++	0	..	..	..	..	..
B. enteritidis	8	+++	+++	+++	+++	+++	+++	+++	0	+	+++	+++	+++	+++	+++
B. subtilis	4	−	−	..	..	+++	−	−	−	−	−	−	−	−	±
	13	−	−	..	..	+++	−	−	−	−	−	−	−	−	−
B. pyocyaneus	7	−	−	..	..	+++	−	−	−	−	−	−	−	−	−

DIPHENYLAMINS.

Thiasins and Thiasons.							Eu-rhodins.	Indulins and Indones.							
Ethylene blue.	Toluidin blue.	Methylene green.	*Thiocarmin, R.*	Methylene violet.	Methylene azure.	Uranin blue.	Neutral red.	Naphtazin blue conc.	Naphtazin blue 3157	Indazin, M.	Paraphenylene blue.	Azin red 5 RN.	*Indulin, R.*	*Indulin, B.*
+++	+++	+++	+++	± to +	+++	+++	+++	+++	+	0	+++	+++	+++	+++
+++	+++	+++	+++	+++	+++	+++	+++	+++	± to ++	+	..	± to +	+++	+++
+++	+++	+++	+++	++	+++	+++	+++	+++	+	0 to ±	+++	+++	+++	+++
+++	+++	+++	+++	+	+++	+++	+++	+++	+++	0	..	+++	+++	+++
+++	+++	+++	+++	−	+++	+++	+++	+++	.	0 to ±	..	+++	+++	+++
+++	+++	+++	+++	−	+++	+++	+++	+++	+++	0	..	+++	+++	+++
+++	+++	+++	+++	++	+++	+++	+++	+++	+	+	..	+++	+++	+++
−	−	−	−	−	−	−	−	−	−	−	..	−	−	−
0	+++	+++	+++	−	++	+++	+++	+++	++	0	..	++	+++	++
−	+++	−	−	+++	0	+	+++	+++	+++	+	..	++	+++	++
0	+++	+++	++	+++	+++	+++	+++	+++	0	0	+++	0	++	++
0	+++	+++	+++	+++	+++	+++	+++	+++	0 to +	0	..	0	+++	++
+++	+++	+++	++	+++	+	+++	+++	+++	+++	0	..	0	++	++
0	++	+++	± to +	+++	+	+++	+++	+++	++	0	..	0	++	++
−	−	−	−	−	−	−	−	−	−	0	..	0	−	−
0	+++	+++	+++	++	+	+++	+++	+++	++	0	..	0	+++	++
−	−	−	+++	−	−	−	−	+++	−	0	..	0	−	−
−	−	−	−	−	−	+++	−	+++	0	0	..	0	+++	++
+++	+++	+++	+++	−	+++	+++	+++	+++	+++	+ to ++	+++	+++	+++	−
0	+++	+++	+++	−	++	+++	+++	+++	+	0	+++	0	+++	++
0	+++	+++	+++	−	++	+++	+++	+++	+	0	..	0	+++	++
+	+++	+++	++	0	+	+++	+++	+++	+++	0	..	+	+++	++
+	+++	+++	+++	0	+++	+++	+++	+++	0 to ±	0	..	+++	+++	++
0 to ±	++	+++	+++	++	0	+++	+++	+++	+	−	+++	±	+++	++
−	−	−	−	−	−	−	−	+++	+	+++	..	0	+++	++
−	−	−	−	−	−	−	−	+++	0	0	..	±	+++	++
0	+++	−	++	−	0	+++	−	+++	++	−	..	0	+++	−
−	−	−	−	−	−	−	−	+++	++	−	..	−	−	−
−	−	−	−	−	−	−	−	+++	0 to ±	−	..	−	+++	++
+++	+++	+++	+++	±	0	+ to ++	+++	+++	+	0	+++	0	+++	++
+++	+++	+	+++	0	++	+++	+++	+++	+++	0	..	0	+++	++
+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	..	+++	+++	++
+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	..	+++	+++	++
0	++	+++	+++	++	+++	+++	+++	+++	+++	+++	..	+++	+++	++
+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	..	+++	+++	++
+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	..	+++	+++	++
+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	..	+++	+++	++
+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	..	+++	+++	++
+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	..	+++	+++	++
+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	..	+++	+++	++
+++	+++	+++	+++	+++	0 to +	+++	+++	+++	+++	+++	..	+++	+++	++
+++	+++	+++	+++	+++	0 to +	+++	+++	+++	+++	+++	..	+++	+++	++
−	−	−	−	−	−	+++	−	−	−	−	..	+	−	−
−	−	−	+	−	−	−	−	−	−	−	..	0	−	−
−	−	−	−	−	−	+++	−	−	−	+++	..	−	−	−

DIPHENYLAMINS (Continued).

		Safranins and Safranoles.					Aposafranins.				Simple azo anilins and Naph-				
		Phenosafranin.	Tolusafranin.	Tannin-heliotrope.	Amethyst.	Echt neutral violet.	Neutral blue.	Basel blue, R. conc.	*Rosinduline, 2 B.*	*Rosindoline, 2 G.*	Anilin yellow.	*Methyl orange.*	Chrysoidin.	Vesuvin.	*Orange, G.*
St. aureus	1	+++	+++	+++	+++	+++	+++	++	+++	+++	+++	+++	+++	+++	+++
	40	+++	+++	+++	+++	± to +	..	++	+++	+++	..	+++	+++	+++	+++
	42	+++	+++	+++	+++	0 to ±	..	+	+++	+++	+++	+++	+++	+++	+++
	95	±	+++	++	+++	0	..	+++	+++	+++	..	+++	+++	+++	+++
	96	±	++	+	+++	0 to ±	+	+++	+++	+++	..	+++	+++	+++	+++
	53	+++	+++	+	+++	+++	..	+	+++	+++	+++	+++	+++	+++	+++
	84	+++	+++	+++	+++	+	..	+++	+++	+++	..	+++	+++	+++	+++
	58	+++	+++	±	−	0	..	+	+++	+++	+++	−	−	−	−
	83	+++	+++	+++	+++	0 to +	..	+++	+++	+++	..	+++	+++	+++	+++
St. pyogenes	93	−	−	+++	0	+++	..	+++	+++	+++	..	−	+++	−	−
	54	+++	0	0	+++	++	+++	+++	+++	+++	..	+++	+++	+++	+++
	85	+++	++	0	+++	+++	..	+++	+++	+++	..	+++	+++	+++	+++
	92	0	+++	0	+++	+++	..	+++	+++	+++	..	+++	+++	+++	+++
	50	0	−	0	+++	+	+++	+++	+++	+++	+++	+++	+++	+++	+++
	81	± to +	+++	0	+++	+++	..	+	+++	+++	+++	+++	+++	+++	+++
	77	0	0	0	++	+++	..	+++	+++	+++	+++	+++	+++	+++	+++
	78	0	0	0	+++	+++	..	−	+++	+++	..	−	−	−	−
	37	+++	+++	+++	+++	+++	+++	+++	+++	+++	..	+++	+++	+++	+++
	16	+++	+++	+++	+++	+++	+++	+++	+++	+++	..	+++	+++	+++	+++
St. citreus	44	+	+	0 to ±	++	0 to ±	..	0 to ±	+++	+++	+++	+++	+++	−	+++
M. aurantiacus	9	0 to ±	−	0	+++	0	..	+	+++	+++	+++	+++	+++	+++	+++
M. catarrhalis	6	+++	+++	0	+++	0	..	0 to +	+++	+++	..	+++	+++	+++	+++
	75	+++	+++	+	0	++	..	−	+++	−	+++	−	+++	−	+++
	41	..	..	0	−	−	..	0	+++	−	..	+++	−	−	−
	100	++	++	±	+++	0	+	0	+++	+++	+++	+++	−	+++	+++
Pneumococcus	101	+++	−	−	−	+	..	−	+++	+++	−	−	−	−	−
	102	−	−	−	−	−	..	−	−	−	+++	−	+++	+++	+++
Meningococcus	71	+++	−	−	++	−	..	−	++	+++	−	−	−	−	−
Anthrax	14	+++	+++	0 to ±	+++	0	+++	+ to ++	+++	+++	+++	+++	+++	+++	+++
Actinomyces	15	++	+	0 to ±	++	0 to +	..	..	+++	+++	+++	+++	+++	+++	+++
B. typhosus —α	3	+++	+++	+++	+++	+++	..	+++	+++	+++	+++	+++	+++	+++	+++
B. paratyphosus —β	11	+++	+++	+++	+++	+++	..	+++	+++	+++	+++	+++	+++	+++	+++
	12	+++	+++	+++	+++	−	..	+++	+++	+++	+++	+++	+++	+++	+++
B. paracoli	19	+++	+++	+++	+++	++	..	+++	+++	+++	..	+++	+++	+++	+++
B. coli	32	+++	+++	+++	+++	+++	..	+++	+++	+++	..	+++	+++	+++	+++
B. enteritidis	8	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
B. dysenteriæ	67	+	+++	+++	+++	+++	..	+++	+++	+++	+	+++	+++	+++	+++
	68	+	+++	+++	+++	+++	..	+++	+++	+++	++	+++	+++	+++	+++
	69	+++	+++	+++	+++	+++	..	+++	+++	+++	++	+++	+++	+++	+++
	70	+++	+++	+++	+++	++	..	+++	+++	+++	+	+++	+++	+++	+++
	90	+++	−	−	+++	+++	..	+++	+++	+++	−	+++	+++	+++	+++
	91	−	−	−	−	+++	..	+++	+++	+++	−	−	−	−	−
B. subtilis	4	−	−	−	−	−	..	0	−	+++	−	−	−	−	−
	13	−	−	−	−	−	..	−	−	+++	−	−	+++	−	−
B. pyocyaneus	7	−	−	−	−	−	..	−	−	−	−	−	−	−	−

AZO DYES.

thylamins.		Chromotropes.			Azodiphenylamins.	Diazo bodies.		Hydrazones.	Azo benzidins.						Oxyquinones.	
Ponceau.	*Roccellin.*	*Diamil red.*	*Diamil blue.*	*Diamil black.*	*Citronin, 000.*	*Indoin blue.*	*Diazin blue, BR.*	*Tartrazin.*	*Pyramin orange.*	*Congo red.*	*Benzopurpurin.*	*Diazin.*			*W.S.*	*Alizarin blue.*
												Green.	*Blue.*	*Violet.*		*BB.*
+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++

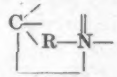
Behavior of the Acid Dyes. A survey of these tables will show that not a single one of the acid dyes proper possesses any inhibitory properties in the standard concentration of 1 to 100,000 which we employed. In a number of instances, indeed, we received the impression as though a favoring effect were exercised upon the growth of those organisms, which ordinarily are inhibited by the triamino-triphenyl methanes. This seemed notably the case with tartrazin, a strongly acid hydrazone; then with Ponceau, an azo dye; further with gallocyanin, an oxazon, and the same had previously been noted in one of the triphenyl methanes, that is, roth violet 5 RS. So manifest was this favoring influence in the case of streptococci that the thought suggested itself that tartrazin agar especially might well be utilized for the routine cultivation of these organisms. Even the meningococcus grows in great abundance on this medium, and for a time we were in hopes that it might take the place of serum agar in the case of this organism. We found, however, to our disappointment that while a number of generations may thus be cultivated without any difficulty the organism sooner or later dies out. The observation seemed interesting in principle nevertheless, and seems worthy of further investigation.

Behavior of Basic Dyes. While the rule which was found to hold good in the case of the triphenyl methanes thus seems to apply to all classes of anilin dyes, namely, that the presence of acid auxochromic groups *per se* in predominating number over any basic groups is incompatible with the existence of any inhibitory properties, it does not follow, as we have already seen in the case of the triphenyl and diphenyl methanes, that basicity on the part of a dye of necessity carries with it inhibitory properties. We thus find in the present series that toluidin blue, methylene green, neutral red, anilin yellow, chrysoidin, and vesuvin exhibit no inhibitory power whatever in the concentration which we have employed. On the other hand, it will be seen that the majority of basic dyes possess inhibitory power of a kind, but only in a few is this so extensively developed as in the triamino-triphenyl methanes, and is frequently directed only against a certain group of organisms. Basel blue was thus found to be active only in the case of certain catarrhal micrococci, and to a certain extent also in the case of the Staphylococcus citreus. The same was noted in the case of diazin blue. Methylene violet affected only the anthrax bacillus, actinomyces, a single strain of the catarrhal micrococcus, and the Micrococcus aurantiacus.

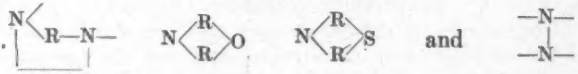
In the case of the triphenyl methanes already it was noted that while some of the dyes were inhibitory for both staphylococci and streptococci, others showed a special selective action for streptococci, while on staphylococci they exercised little or no inhibition. In the groups with which we are dealing in the present

paper this was even more marked, and of the entire number of basic dyes only two were markedly inhibitory for both Staphylococcus aureus and streptococci, namely, indazin M and new methylene blue, while echt neutral violet seemed to have a special affinity for staphylococci and azin red, tannin heliotrope, pheno- and tolusafranin, capri blue and coelestin blue, ethylene blue and methylene blue were inhibitory only for streptococci and catarrhal micrococci. As far as the anthrax bacillus and actinomyces are concerned, these were inhibited by practically every dye that had any inhibitory power upon staphylo- or streptococci.

Relation of Chromophoric Group to Inhibition. The fact that so many of the triphenyl methane derivatives are endowed with inhibitory properties strongly suggests that the underlying chromophoric group, which according to Witt is here the complex



(where R represents a benzene radicle) may be responsible for this effect. The thought, hence, suggests itself that in the other inhibitory dyes of basic nature also the chromophore may be operative in this respect. If further investigation should prove this to be the case, we would be forced to the interesting conclusion on the basis of our own observations that of the enormous number of anilin dyes only those can be expected to have inhibitory properties in which the groups



are represented.

Nature of the Inhibitory Action of the Dyes in Question. In considering the nature of the inhibitory action of the dyes in question two possibilities immediately suggest themselves, namely, the existence of a physical as contrasted with a chemical interaction between the dye and the microörganism. As we have shown in our first communication, Stilling inclined to the first possibility, although he felt that chemical influences could not be excluded in the production of the death of the organism. To this view he was without doubt led in great part by the observation that in sufficient concentration the dyes which he had studied would prevent the development of practically all the different bacteria with which he was dealing. But with this phase of the problem we are hardly concerned. On the contrary, we are interested primarily in the fact that in certain dilutions certain dyes will only inhibit the growth of certain organisms. This fact was first pointed out by Rozsahegyi, and was then made the subject

of an extended investigation, in reference to one of the most active dyes in this respect, namely, gentian violet, by Churchman. As a result of his investigations, he divides bacteria into a violet positive and a violet negative group. We have shown that these terms have not been well chosen, since the violet color of the dye has really nothing to do with its inhibiting character, but the fact remains that certain organisms are inhibited by certain dyes, while in others there is no evidence of such an inhibition whatsoever (in the concentration 1 to 100,000 chosen by Churchman and myself as standard). This fact in itself, irrespective even of the important bearing of the basicity or acidity of the dye, makes it seem *a priori*, unlikely that the effects should be of a physical character only. But even more significant in this respect is the fact that certain representatives of a susceptible group of organisms which otherwise present the same morphological and cultural characteristics as the remainder may be dye fast, that is, they are not inhibited by those dyes which interfere with the development of the other members of the same group.

NATURAL DYE-FAST STRAINS. Churchman already noted an instance of this nature, for he mentions that "in a study of five nearly identical strains belonging to the enteritidis group the selective affinity of the stain (gentian violet) was found to be so specific in its nature as to distinguish between different strains of closely related organisms. On the growth of one member of this group the dye exhibited a constant and complete inhibition; on the other four it was absolutely without any effect."

This differing susceptibility of different members of a given group of organisms to a given dye we could establish also in the case of the staphylococci, the streptococci, and the pneumococci. This is illustrated in Table I, in reference to crystal violet agar (sc., serum agar in the case of the pneumococci), 0 indicating absence of growth, ± faint growth, and +++ abundant growth, as in our first paper.

TABLE I.—Showing the behavior of different strains of staphylococci, streptococci, and pneumococci in reference to crystal violet (1 in 100,000).

Staphylococcus aureus.								
(1)	(40)	(42)	(53)	(58)	(83)	(84)	(95)	(96)
0	0	0	+	0	0	±	0	0

Staphylococcus Citreus.
(44)
0

Micrococcus Aurantiacus.
(9)
+ to ++

Streptococcus Pyogenes.											
(92)	(26)	(28)	(54)	(43)	(50)	(81)	(77)	(61)	(78)	(16)	(37)
++	0	0	++	0	0	0	0	0	0	+++	0

Diplococcus Pneumoniæ.			
(102)	(64)	(29)	
0	+	0	

TABLE II.—Showing the behavior of different strains of staphylococci and streptococci toward various inhibitory dyes.

	Staphylococcus aureus.						Micrococcus catarrhalis.		Streptococcus pyogenes.					
	(1)	(40)	(95)	(42)	(53)	(84)	(100)	(6)	(92)	(85)	(50)	(77)	(16)	(37)
Methyl violet	0	0	0	0	0	0	–	0	0	0	0	+++	+++	0
Crystal violet	0	0	0	0	+	0	–	0	++	0	0	0	+++	0
Hofmann's violet	0	0	0	0	0	±	0	0	++	0	0	+++	+++	0
Benzyl violet	0	0	0	0 to ±	0	0	±	0	0	0	0	0	+++	0
Dahlia	0	±	0	0	0	0	0	0	+++	0	0	+++	+++	0
Fuchsin	0	+++	+++	0	+++	+++	+++	0	+++	0	0	+++	+++	0
New fuchsin	0	0	+++	0	+++	0	0	0	+	0	0	+++	+++	0
Ethyl green	+	+	+ to ++	++	++	0	0	+	0	0	0	0	+++	0
Brilliant green	+++	+	+	0 to ±	+++	0 to ±	0 to ±	++	+	0	0	0	+++	0
Rhodamin 3B	0	0	±	+	+	±	0	+++	++	+++	+++	+++	+++	+++
Rosazin B	0	0 to ±	0	0	0	0	0	0	+ to ++	++	0	0	+++	0
Indazin M	0	++	0 to ±	0	0	0 to ±	–	0	0	0	0	0	+ to ++	0

This difference in behavior is even more strikingly seen in connection with some of the other inhibitory dyes, as is illustrated in Table II, which likewise shows that even though some of these dyes are closely related, they do not behave in the same manner toward all the strains (see also collective tables).

To explain these individual peculiarities upon a purely physical basis would certainly be difficult, and we are inclined to lay special stress upon this factor as favoring the view that the inhibitory action is of a chemical nature. The likelihood that this may be the case is further emphasized by our observation that it is possible to produce dye-fast strains artificially.

Artificial Production of Dye-fast Strains. The observation of Churchman that one single strain only of the B. enteritidis group which he had studied was dye-labile, and our own findings of the occasional deviation from what seems to be the normal for a given group of organisms in reference to a given dye, suggested the idea that this aberration might be viewed as a mutation the outcome of special nutritional conditions, and that it should be possible to produce such mutation artificially. We accordingly planted representatives of the different groups of organisms, which collectively were found to be dye-labile upon agar containing the inhibitory dye, in a dilution of 1 in 10,000,000, and increased this gradually (the rate of progress being determined by the activity of the growth) until the 1 in 100,000 standard was reached. A series of experiments of this order and the ultimate results are shown in Table III.

Table III.—Showing the gradual adaptation of different organisms to crystal violet.

Behavior toward	Bacillus subtilis. (4)	Bacillus enteritidis. (8)	Staphylococcus aureus. (42)	Staphylococcus aureus. (1)	Bacillus anthracis. (14)
1 in 100,000 (initial)	0	±	0	0	0
1 in 10,000,000	+++	+++	+++	+++	+++
1 in 9,000,000	+++	+++	+++	+++	+++
1 in 8,000,000	+++	+++	+++	+++	+++
1 in 7,000,000	+++	+++	+++	+++	+++
1 in 6,000,000	+++	+++	+++	+++	+++
1 in 5,000,000	+++	+++	+++	+++	+++
1 in 4,000,000	+++	+++	+++	+++	+++
1 in 3,000,000	+++	+++	+++	+++	+++
1 in 2,000,000	+++	+++	+++	+++	+++
1 in 1,000,000	+++	+++	+++	+++	+++
1 in 900,000	+++	+++	++	+++	+++
1 in 800,000	+++	+++	++	++	+++
1 in 700,000	+++	+++	++	++	+++
1 in 600,000	+++	+++	++	++	+++
1 in 500,000	+++	+++	++	++	++
1 in 400,000	+++	+++	+	++	++
1 in 300,000	++	+++	+	+	+
1 in 200,000	++	+++	+	+	+
1 in 100,000	++	+++	+	+	±

While these experiments unquestionably demonstrate the possibility of producing dye-fast strains artificially, it must be admitted that the extent to which this is possible is extremely variable. In the case of the subtilis and the enteritidis strain (of the table) it was merely a matter of transplanting daily to the next strength of agar, while with the other three organisms it was sometimes necessary on entering the higher concentrations to allow growth to continue for a few days in the same concentration before advancing to the next. As the end-result shows the degree of adaptation was also quite variable, and in some instances the 1 in 100,000 mark could not be reached.

In this connection it may be interesting to point out that the B. enteritidis (8) strain which during the greater part of the winter had been dye-labile ultimately became dye-stabile, that is it finally grew quite readily in the presence of all those dyes which in the early fall had inhibited its growth. We cannot help but feel that this change must be viewed as a reversion to what, for that group of organisms, seems to be the normal state. Similarly, we have noted that one streptococcus (16) which originally grew most luxuriantly in the presence of the common inhibitory dyes, is now inhibited by some members of this group (Table IV).

TABLE IV.—Showing reversion of two bacterial strains.

	Original behavior.			Present behavior.		
	Methyl violet.	Dahlia.	Brilliant green.	Methyl violet.	Dahlia.	Brilliant green.
Bacillus enteritidis (8)	0	0	−	++	+++	−
Streptococcus (16)	+++	+++	+++	0	0	0

Upon thinking over the possibilities which have led to this altered behavior we are inclined to refer the change to the fact that whereas during the fall and early winter months the stock cultures of these organisms had been grown on plain agar, they had later been cultivated on beef-juice agar. That apparently insignificant changes in the nutritional surroundings of an organism may actually lead to marked changes in the response of the organism to nutritional stimuli is also shown by an incidental observation which we made when a certain strain of the catarrhal micrococcus had been grown for a comparatively brief period of time on corallin agar and was then transplanted to plain agar and this culture compared with the original (which had not been growing in the presence of corallin). The results are seen in Table V.

TABLE V.—Showing mutation of a catarrhal micrococcus strain under the influence of corallin.

	Methyl violet.	Crystal violet.	Hofmann's violet.
Behavior of original culture (75)	0	0	0
Behavior of culture after having been subjected to influence of corallin (75c)	++	++	+++

If now we attempt an explanation of these various phenomena, namely, the inhibitory action of certain dyes, the existence of natural dye-fast strains, and the possibility of the artificial production of dye fastness, we must bear in mind the fundamental fact that only basic dyes may exhibit inhibitory properties. The most plausible inference, hence, would be to assume the existence of corresponding acid groups in the structure of the organisms in question, with which these basic groups would tend to unite, possibly in a manner corresponding to our concept of the structure of peptids. We could then conceive that the microörganism having anchored the dye in this manner now finds itself unable to bring about the destruction of the molecule with the consequent liberation of that portion which it could utilize in its own metabolism, and the restitution of its own combining receptors. We would thus explain the phenomenon of dye susceptibility upon the same basis upon which Ehrlich explained the action of the toxin molecule upon a cell provided with corresponding receptors, without the necessity, however, of assuming a directly toxic influence. In other words, the cell dies, not necessarily because it has been poisoned, but because a sufficient number of its nutriceptors have been thrown out of action to bring about its starvation, or inability to multiply, as the case may be. This hypothesis would also explain why an acid dye of otherwise the same structure as the corresponding basic inhibitory dye, even though the same number of amino groups should be present, does not interfere with the growth of the organism. For we could readily conceive either that the dye might be anchored by both its basic and acid groups, or if the latter only should be present, by these alone, and that the attack upon or through this group would lead to the destruction of the molecule, and the liberation of the corresponding receptors. In this connection it may not be out of place to refer to the recent observations by Berthelot and Bertrand[3] on the behavior of a certain bacillus, which was isolated by them from the feces, and which was shown to be able either to remove the amino group or the carboxyl group from certain amino-acids and peptids, or both at the same time, according to the nature of the nutritive elements which were otherwise placed at its disposal, showing that the successful attack upon a certain group may lead to the destruction of the nutrient molecule, but that this does not follow of necessity. This is quite in accord with the hypothesis set forth above that the presence of the acid auxochromic group may enable the organism to successfully attack the amino group also, while in the presence of the latter alone this may not be possible. Further investigations will, of course, be necessary

[3] A. Berthelot and D. M. Bertrand, Sur quelques propriétés biochimiques du b. aminophilus intestinalis, Compt. rend. acad. sci., 1912, cliv, No. 26.

to establish the validity of the explanation which has been offered, but it affords even now a possible explanation, where otherwise it would be difficult to account for the observed facts.

The question, then, whether or not a given organism will be inhibited in its growth by a certain dye would, according to our hypothesis, depend primarily upon the existence of suitable receptors on the part of the organism, and secondarily upon its ability to bring about the liberation of such receptors after once they have been occupied by the dye. To these factors two additional ones should be added, namely, the existence or non-existence of other receptors by which the organism could carry on its nutrition (sc., reproduction), and the possibility of producing such receptors, while the others are occupied by the dye.

Upon the preponderance of susceptible receptors over others, or the relative proportion of these, as compared with others that might serve the purpose of nutrition, the extent of the inhibitory effect would, of course, depend, and account for the divers results that have been obtained in our investigations and which are illustrated in the various tables.

The fact that certain strains of an otherwise dye-susceptible group exist in nature or may be produced artificially would seem to warrant the assumption that such receptors either occur preformed or may be produced artificially, and is in itself a support of our hypothesis, and perfectly in accord with the observations of Ehrlich on the occurrence or production of arsenic-fast strains of trypanosomes. Hitherto we have known but little of the possible existence or production of drug-fast bacteria, and so far as our knowledge goes, Morgenthal's observations on the production of drug-fast pneumococcus strains in the animal experiment are the only ones besides our own which go to show that the principle involved applies not only to animal but also to vegetable organisms.

Should our interpretation of the phenomena under investigation be ultimately proved to be correct in principle, even though not in detail, the chemical nature of the inhibitory action of the dyes would seem to be established. At present we think that the evidence which we have furnished points in that direction.

SUMMARY. 1. The inhibitory action upon the growth of certain bacteria which has been shown to be common to all the triaminotriphenyl methanes is not an exclusive property of this group of anilin dyes, but manifested also to a greater or less extent by other strongly basic dyes, and is dependent upon the presence of basic auxochromic groups and the absence of corresponding acid groups (sc., a preponderance of the former over the latter), in association with the existence of certain chromophoric radicles.

2. Some members belonging to dye-susceptible groups of organisms exist in nature which are not inhibited by the dyes in question.

3. Dye susceptibility may be overcome to a greater or less extent by adaptation.

4. The inhibitory action of the dyes in question is probably due to the existence of corresponding (nutri?) receptors in the microörganism to which the dye is anchored, and its inability to bring about the destruction of the dye and the consequent liberation of the corresponding receptors.

5. Natural or artificial adaptation is due to the production of different receptors by which the nutrition (sc., reproduction) of the organism can be carried on, and which either possesses no affinity for the dye in question, or through which the organism can bring about its destruction.

Since writing the above the artificial production of dye-fast strains of bacteria has also been announced from Ehrlich's laboratory.[4]

DIAGNOSTIC VALUE OF PERCUTANEOUS TUBERCULIN TEST (MORO).

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The specificity of the cutaneous tuberculin reactions is well established;[1] in other words, it is generally acknowledged that a positive reaction to a tuberculin test indicates a previous tuberculous infection, with the production of tuberculous antibodies. For most clinicians, however, and this apparently applies especially to tuberculosis specialists, the extreme sensitiveness of the reaction, whereby even unsuspected or long-cured cases react positively, militates against its practical importance in clinical medicine. Believing that practically all adults have been at one time or another infected by the tubercle bacillus sufficiently to give a positive reaction, they consider such a reaction to be of little use after infancy and of no value in adult life. For instance, Lawrason Brown says: "A positive reaction (of the cutaneous test) after seven or eight years is of little value, as tuberculous infection and clinical tuberculosis are vastly different." This sentiment is so widespread

[4] Ueber Gewöhnung d. Bakterien au Farbstaffe. Shiga klin. Zeitsch. f. Immunitätsforsch., vol. xviii, p. 65.

[1] Lawrason Brown, Amer. Jour. Med. Sci., 1911, cxli, 469; L. Hamman and S. Wolman, Arch. Int. Med., 1910, vi, 690, et al.

that it is safe to say that, in spite of the admitted value of negative reactions, the use of the various tuberculin tests is not spreading with the rapidity that such valuable diagnostic agents deserve.

Granting that these tests fail to differentiate between the so-called "clinical" and "non-clinical tuberculosis" (an infection never giving rise to noticeable signs or symptoms), we nevertheless believe that the idea that almost all adults will give a positive reaction is erroneous. Whether or not this belief contradicts the theory that almost all adults have been infected at one time or another with tuberculosis, or whether, as some have suggested, it means that a healthy person who has long overcome a tuberculous infection, eventually may lose his sensitiveness so that the positive reaction may "fade"[2] and eventually change to negative, we are unable to say. The fact, however, remains, as ours and other figures will show[3] that in an unselected series of non-tuberculous subjects a small proportion may react positively. It therefore follows not only that the negative reaction with certain definite qualifications practically excludes tuberculosis, but also that the positive reaction is of value, in adults as well as in children, in indicating if not the exhibition of an active course of treatment against clinical tuberculosis, at least an extremely cautious attitude (hygienically and prophylactically) toward the known subject of a tuberculous infection. The unfavorable critique of the tuberculin reactions is well given by M. R. Pla y Armengol.[4]

The following series of 149 cases were seen by us mostly in the wards and out-patient department of the Pennsylvania Hospital during a period of over three years. The Moro[5] percutaneous test was selected on account of the freedom from infection and discomfort and ease of application. In 128 cases it was controlled by simultaneous applications of the von Pirquet test, applied in the usual manner. This, in the main, agreed with the results of the Moro test, but in a few cases was apparently even more sensitive.[6] As the chief objection to these tests is their hypersensitivity, this greater sensitivity of the von Pirquet test should be rather considered an objection than an advantage. As the Moro test apparently does not fail to react on tuberculous subjects (with certain known limitations), it would seem to be preferable.

The test was performed substantially as originally described by Moro: a part of the skin free from hair (in epigastrium or hypochondrium), about the size of a silver dollar, is cleaned first with alcohol then with distilled water; one-half the contents of a tube of Moro tuberculin paste (old tuberculin in a base of lanolin, as prepared by

[2] L. Hamman and S. Wolman, Arch. Int. Med., 1910, vi, 690.

[3] F. L. Wachenheim, Amer. Jour. Dis. of Child., 1912, iv, 27, and 1913, v, 466; J. W. Bride, British Med. Jour., May 14, 1910, p. 1161; T. Mills, ibid., p. 1159; M. Pelm, Lyon Med., 1911, cxvii, 945; A. Radsiejweski, Zeitsch. f. Kinderheilk, Orig., 1911, ii, 520, et al.

[4] Presse Méd., 1911, xix, 857.

[5] Münch. med Woch., 1908, lv, 216.

[6] Compare findings of E. Emmerich, Münch. med. Woch., 1908, lv, 1066.

Mulford), about the size of a large pea, is rubbed in vigorously for two minutes. In a similar control area a similar amount of lanolin (the base of the paste) is rubbed for an equal length of time. Both are protected by waxed paper and a dry gauze dressing. In no case was the slightest discomfort, either local or general, experienced. (After the first fifty of these controls had uniformly proved negative the control test was abandoned.) A typical small papular rash (20 to 200) was considered positive; no change as negative; and all other changes as doubtful. If the person administering the test does not react positively himself, it can more conveniently be applied with the bare finger, a rubber finger-cot may be used if preferred.[7]

A positive reaction appeared in the first twenty-four hours in the majority of cases, though in some it did not appear for forty-eight hours; in 2 cases it was negative in forty-eight hours, and typically positive in seventy-two hours; in one case it did not appear until the sixth day. The tests being performed indiscriminately on ward and dispensary patients, were mostly on adults, and therefore constitute a severer trial than if done on children. Before the statistics were arranged, an attempt was made to find out, by mail and by visiting, the subsequent history of the cases, many dating back two and three years. The floating nature of our dispensary population, however, prevented us from reaching more than 12 per cent. The data thus obtained was incorporated in the tables, and was of use in the ultimate diagnosis.

The 149 cases examined have been divided more or less arbitrarily into six classes: three grades of pulmonary tuberculosis (first, incipient or arrested; second, moderately advanced, third, far advanced); other forms of tuberculosis (pleurisy, meningitis, coxitis, etc.); doubtful tuberculosis; and non-tuberculosis (normal and diseases in which tuberculosis could be excluded). The first grade may be assumed to be more or less sensitive (that is, to possess free antibodies which will react to the test), the second still more sensitive; whereas in the third grade the overwhelming infection may be considered so to have exhausted the patient that he frequently is no longer able to produce antibodies which will react to the test. Hence the large proportion of negative reactions in this class. In the last class were put all cases that were definitely non-tuberculous. If any doubt arose, though the tests may have turned out negative, they were included in the doubtful class; conversely, apparently tuberculous cases about which doubt existed were also put in the doubtful class. In diseases like pleurisy, bronchitis, and bronchopneumonia, unless there was a sufficiency of reliable symptoms, such as predominance of certain cells in the

[7] As one of the authors was found to respond positively to the test, several different samples were tried on him, at various times, and all were found to react positively.

exudate, previous and family history, course of illness, and so forth, the case was put in the doubtful class, always, of course, without regard to the outcome of the test.

TABLE I.—Incipient or Arrested Cases of Pulmonary Tuberculosis.

Case No.	Date of test.	Name.	Result.	Remarks.
2	July 14, 1909	Solomon A.	Positive	Convalescent typhoid; dulness and slight deformity of right apex; prolonged, sighing expiration.
14	Aug. 23, 1909	Myer A.	Positive	Von Pirquet also positive; convalescent typhoid; chronic cough; rales and dulness at left apex; brother had tuberculosis.
15	Aug. 23, 1909	Tony Z.	Positive	Chronic cough; rales and dulness at left apex and base.
50	Sept. 20, 1909	Salvatore F.	Positive	Von Pirquet also positive.
80	Sept. 25, 1909	Celia K.	Positive	Von Pirquet also positive; signs of lesion at right apex; lost weight.
86	Oct. 5, 1909	Theresa K.	Positive	Von Pirquet also positive; slight signs at right apex.
112	Mar. 5, 1912	Sam. A.	Positive	Cough; pain in chest; signs at right apex.
113	Mar. 21, 1912	Norman C.	Positive	Von Pirquet also positive; in March, 1913, after continuous outdoor treatment, gained weight; no cough; no signs in lungs.
115	May 4, 1912	Sam. B.	Positive	Cough for five years; signs at left apex.
116	May 7, 1912	Katie J.	Positive	Cough for three years; occasionally chilly and dyspneic.
126	Sept. 3, 1912	Frank C.	Positive	Cough; presternal pain for two weeks; signs at right apex.
134	Aug. 10, 1912	Mary P.	Positive	Fever; cough; rales; loss of weight; improved greatly under treatment; in March, 1913, found at home moribund, general involvement, etc.
137	April 28, 1913	Joseph W.	Positive	Negative on first day; positive on fifth day; signs at right apex; leukocytes, 15,200.
131	Aug. 20, 1912	Alex. S.	Positive	Had pain for three months; cough; rales above and below both apices; dulness at right apex.

14 cases, all positive.

TABLE II.—Moderately Advanced Pulmonary Tuberculosis.

Case No.	Date of test.	Name.	Result.	Remarks.
1	July 14, 1909	Joseph D.	Positive	Marked signs at left apex; bloody sputum.
56	Aug. 2, 1909	Jim. C.	Positive	Calmette also positive; right apical lesion with deformity.
70	Oct. 3, 1909	Louis G.	Positive	Von Pirquet also positive; lesion of right lung.
81	Sept. 22, 1909	Costansa C.	Positive	Von Pirquet also positive.
82	Sept. 29, 1909	Minnie T.	Positive	Von Pirquet also positive; rales; dulness at right apex; tubercle bacilli in sputum.
97	Jan. 27, 1910	John J.	Positive	Von Pirquet also positive; cough; fever; diarrhea; signs in lungs.
127	Aug. 14, 1910	Hyman L.	Positive	Diagnosis confirmed at Phipps Institute; in March, 1913, about the same.
135	April 28, 1913	William C.	Positive	Negative on first day; leukocytes, 11,000.
138	May 2, 1913	Frank L.	Positive	Negative on first day; leukocytes 9200 before, 10,200 after.
140	May 2, 1913	Mrs. K. K.	Positive	Negative on first day; leukocytes, 14,000 before, 10,000 after.

10 cases, all positive.

TABLE 3.—Advanced Pulmonary Tuberculosis.

Case No.	Date of test.	Name.	Result.	Remarks.
6	July 26, 1909	John S.	Negative	Cavities developed during acute febrile course; confirmed at autopsy two months later.
39	Sept. 4, 1909	Ed. R.	Negative (twice)	Von Pirquet once positive; active and extensive involvement; pulmonary hemorrhage; tubercle bacilli in sputum.
72	Oct. 3, 1909	John C.	Negative	Von Pirquet negative; far advanced with cavities.
85	Oct. 5, 1909	Mattie E.	Negative	Von Pirquet positive; extensive involvement; tubercle bacilli in sputum.
87	Oct. 5, 1909	Katie L.	Negative	Von Pirquet positive; active, extensive involvement, with fever.
90	Oct. 20, 1909	Hattie B.	Negative	Von Pirquet positive; far advanced, with cavities; confirmed at autopsy.
109	Mar. 8, 1912	John S.	Negative	Lost ten pounds; advanced lesions, with death later, at Pennsylvania Hospital.
118	May 11, 1912	Charles H.	Negative	Also spinal tuberculosis; died in two months.
136	April 28, 1913	William C.	Negative	Far advanced in both lungs; leukocytes, 38,000.
139	May 2, 1913	Charles M.	Doubtful	Slight reaction on third day; disappeared on fifth day; leukocytes 22,600 before, 18,000 after.

Of 10 cases, 9 were negative and 1 doubtfully positive.

TABLE 4.—Other Forms of Tuberculosis.

Case No.	Date of test.	Name.	Diagnosis.	Result.	Remarks.
3	July 26, 1909	Louis M.	Pleurisy	Positive	Long standing; lymphocytes predominant in pleural fluid.
17	Aug. 23, 1909	Tony R.	Meningitis	Positive	Lymphocytes predominant in spinal fluid; no autopsy.
36	Sept. 4, 1909	Charles Z.	Pleurisy	Positive	Subject to coughs; long-standing osteomyelitis; mother has tuberculosis; protracted case; no fluid obtainable.
42	Sept. 4, 1909	Antonio L.	Pleurisy	Positive	Lost twenty pounds; thickened pleura; lymphocytes predominate.
46	Sept. 14, 1909	John di F.	Pleurisy	Positive	Repeated attacks; reaction slight for forty-eight hours, severe in seventy-two hours;
92	Oct. 20, 1909	Benjamin S.	Meningitis	Positive	Von Pirquet also positive; tubercle bacilli in spinal fluid.
105	Feb. 4, 1910	Salvatore C.	Pleurisy	Positive	Von Pirquet also positive; lymphocytes predominate in pleural fluid.
106	Feb 2, 1910	Luigi M.	Pleurisy	Positive	Von Pirquet also positive; not tapped; leukocytes, 7440.
131	Aug. 23, 1912	Ettore P.	Pleurisy	Positive	Several attacks of pneumonia (?) and pleurisy; now rubs and dulness on left side; pain and cough; three months later unchanged.
142	May 10, 1913	Stinger (P. G. H.)	Tuberculosis of hip	Positive	Non-febrile; local pain and swelling.

10 cases, all positive.

TABLE 5.—Doubtful Cases.

Case No.	Date of test.	Name.	Diagnosis.	Result.	Remarks.
28	Aug. 28, 1909	Thomas M.	Acute pleurisy	Negative	"Never sick before;" in second week of illness eloped from hospital.
44	Sept. 14, 1909	Tony B.	Pleurisy; tuberculous	Doubtful (twice)	Sick one month; cough; pain in side; fever; lymphocytes predominant in pleuritic fluid.
48	Sept. 20, 1909	Harry D.	Pulmonary tuberculosis; myocarditis	Positive	Chronic cough (ten years); lost twenty pounds; *x*-rays show apical infiltration; von Pirquet also positive.
49	Sept. 20, 1909	Pietro S.	Lobar pneumonia	Negative	Some delay in resolution; von Pirquet doubtful.
52	Sept. 20, 1909	William S.	Pulmonary tuberculosis (?)	Negative	Chronic cough; occult bloody sputum; night sweats; von Pirquet positive; no tubercle bacilli in sputum.
53	Sept. 28, 1909	Peter M.	Acute articular rheumatism; pulmonary tuberculosis (?)	Negative	Right apex slight dulness and prolonged expiration; von Pirquet positive.
55	Sept. 28, 1909	Chianese M.	Pleurisy	Negative	Second attack; slow recovery; lymphocytes about half; von Pirquet positive.
58	Sept. 15, 1909	Sarah H.	Mitral insufficiency; pulmonary tuberculosis (?)	Positive	Fremitus increased below right clavicle with blowing respiration; autopsy refused; von Pirquet also positive.
68	Oct. 2, 1909	John C.	Pleurisy	Positive	Acute onset; rales at right apex; von Pirquet also positive.
69	Oct. 2, 1909	Nick di M.	Pleurisy	Positive	Chronic thickened pleura; von Pirquet positive.
71	Oct. 3, 1909	Charles S.	Pleurisy	Negative	Von Pirquet positive.
75	Dec. 20, 1909	Joe C.	Polyserositis	Negative	Von Pirquet positive.
76	Dec. 20, 1909	Samuel M.	Pleurisy	Positive	Von Pirquet also positive.
83	Sept. 30, 1909	Sarah B.	Bronchopneumonia	Negative	Von Pirquet positive.
96	Jan. 31, 1910	Daniel P.	Chronic dysentery	Negative	Persistent mucosanguineous diarrhea; improved after returning to Italy; von Pirquet negative. No tubercle bacilli in stools.
100	Jan. 27, 1910	Nick P.	Lobar pneumonia	Negative	Delayed resolution; von Pirquet positive.
101	Jan. 27, 1910	Antonio T.	Pleurisy	Negative	First attack lasted two months; von Pirquet doubtful.
107	Feb. 4, 1910	Tony di J.	Pleurisy	Doubtful	Two years later healthy, but has occasional pains in side; von Pirquet positive.
108	Feb. 22, 1912	Sarah W.	Chronic bronchitis	Doubtful	Fever; sweats; cough; seen only twice.
114	April 5, 1912	Boris P.	Pulmonary tuberculosis (?)	Doubtful	Signs at right apex; cough; chills; sweats; eight months later about the same.
120	June 18, 1912	Enibale G.	Pulmonary tuberculosis (?)	Negative	Cough for four months; pain in left axilla; no fever.
121	Aug. 6, 1912	Harry H.	Pleurisy	Positive	Temperature, 99.3°; cough for one month; rubs at left base and side.
123	Aug. 9, 1912	Leo Q.	Pleurisy	Negative	Pain for three months; tapped one month ago; fluid returned.
124	Aug. 30, 1912	Dominic R.	Chronic pleurodynia	Doubtful	Pain in left side, apparently rheumatic; a few large papules after forty-eight hours.
128	Aug. 17, 1912	Bemjanin C.	Pulmonary tuberculosis (?)	Doubtful	Dry cough (tonsils and adenoids); unchanged six months later.
129	Aug. 17, 1912	Charles D.	Tuberculous pleurisy	Positive	Pain and dry cough for several years.
130	Aug. 20, 1912	Fred. R.	Acute bronchitis	Negative	Rales soon disappeared; neurotic.
141	May 2, 1913	Mrs. L. H.	Acute bronchitis	Negative	Leukocytes 9600 before test, 5800 after.

Of 28 cases by the Moro test, 15 were negative, 6 doubtful (that is, an atypical or scanty eruption appeared), and 7 positive. In the 16 cases in which the von Pirquet tests were made, 9 negative Moros gave 7 positive von Pirquets and 2 doubtful von Pirquets; 1 doubtful Moro gave a positive von Pirquet. The other 6 tallied. This discrepancy has been commented on above.

TABLE 6.—Non-tuberculous Cases.[8]

Case No.	Date of test.	Name.	Diagnosis.	Result.	Remarks.
4	July 26, 1909	Jacob B.	Acute pleurisy	Negative	Quick recovery, polymorphonuclears predominant in pleural fluid.
5	July 26, 1909	Joseph W.	Hemiplegia	Negative	No sign of tuberculosis in history or examination.
7	July 26, 1909	Leon F.	Typhoid	Negative	No sign of tuberculosis in history or examination.
8	July 12, 1909	Charles P.	Malaria	Negative	No sign of tuberculosis in history or examination.
9	Aug. 12, 1909	Lorenzo L.	Typhoid	Negative	No sign of tuberculosis in history or examination.
10	Aug. 12, 1909	John S.	Chronic nephritis	Negative	No sign of tuberculosis in history or examination.
11	Aug. 12, 1909	William S.	Typhoid	Negative	No sign of tuberculosis in history or examination.
12	Aug. 12, 1909	Louis L.	Typhoid	Negative	No sign of tuberculosis in history or examination.
13	Aug. 23, 1909	James D.	Chronic arthritis	Negative	Polymorphonuclears predominant in fluid from knee.
16	Aug. 23, 1909	Pascal D.	Acute pleurisy	Negative	Short attack; polymorphonuclears predominant in fluid from pleural cavity.
18	Aug. 23, 1909	Lawrence C.	Chronic endocarditis	Negative	No sign of tuberculosis in history or examination.
19	Sept. 1, 1909	John Di L.	Plumbism	Negative	No sign of tuberculosis in history or examination.
20	Sept. 1, 1909	James L.	Torticollis	Negative	No sign of tuberculosis in history or examination.
21	Sept. 1, 1909	Joseph C.	Typhoid	Negative	No sign of tuberculosis in history or examination.
22	Sept. 1, 1909	James A.	Typhoid	Negative	No sign of tuberculosis in history or examination.
23	Sept. 1, 1909	Thomas M.	Typhoid	Negative	No sign of tuberculosis in history or examination.
24	Sept. 1, 1909	Steve M.	Typhoid	Negative	No sign of tuberculosis in history or examination.
25	Sept. 1, 1909	Sam L.	Typhoid	Negative	No sign of tuberculosis in history or examination.
26	Sept. 1, 1909	Frank R.	Typhoid	Negative	No sign of tuberculosis in history or examination.
27	Sept. 1, 1909	John A.	Typhoid	Negative	No sign of tuberculosis in history or examination.
29	Sept. 4, 1909	Frank P.	Plumbism	Negative	No sign of tuberculosis in history or examination.
30	Sept. 4, 1909	Angelo M.	Catarrhal jaundice	Negative	No sign of tuberculosis in history or examination.
31	Sept. 4, 1909	William S.	Typhoid	Negative	No sign of tuberculosis in history or examination.
32	Sept. 4, 1909	Nathan F.	Typhoid	Negative	No sign of tuberculosis in history or examination.
33	Sept. 4, 1909	Gennaro D.	Typhoid	Negative	No sign of tuberculosis in history or examination.
34	Sept. 4, 1909	Frank M.	Gastro-enteritis	Negative	No sign of tuberculosis in history or examination.
35	Sept. 4, 1909	William K.	Typhoid	Doubtful	No sign of tuberculosis in history or examination.
37	Sept. 4, 1909	William G.	Asthma	Negative	No sign of tuberculosis in history or examination.
40	Sept. 4, 1909	Nicolo T.	Inguinal hernia	Negative	No sign of tuberculosis in history or examination.
41	Sept. 4, 1909	Joseph S.	Typhoid	Negative	No sign of tuberculosis in history or examination.
43	Sept. 4, 1909	John L.	Lobar pneumonia	Negative	Ran ordinary course, with crisis. No sign of tuberculosis in history or examination.
45	Sept. 14, 1909	John B.	Plumbism; iodism	Negative	No sign of tuberculosis in history or examination.
47	Sept. 14, 1909	Abe T.	Aneurysm of vertebral artery	Negative	No sign of tuberculosis in history or autopsy.
51	Sept. 20, 1912	Louis L.	Paratyphoid	Negative	No sign of tuberculosis in history or examination.
54	Sept. 28, 1909	Paul R.	Lobar pneumonia	Negative	No sign of tuberculosis in history or examination; von Pirquet doubtful.
57	Sept. 15, 1909	Laura S.	Toxic neuritis	Positive	No sign of tuberculosis in history or examination; von Pirquet also positive.

[8] Practically all the tests in the acute infectious cases were done in the convalescent stage

TABLE 6.—(*Continued.*

Case No.	Date of test.	Name.	Diagnosis.	Result.	Remarks.
59	Sept. 15, 1909	Mary S.	Cardiorenal	Negative	No sign of tuberculosis in history or examination; von Pirquet also negative.
60	Sept. 16, 1909	Clarissa N.	Typhoid	Negative	No sign of tuberculosis in history or examination; von Pirquet also negative.
61	Sept. 16, 1909	Elisa S.	Typhoid	Negative	No sign of tuberculosis in history or examination; von Pirquet also negative.
62	Sept. 18, 1909	Maggie G.	Typhoid	Negative	No sign of tuberculosis in history or examination; von Pirquet also negative.
63	Sept. 18, 1909	Joseph C.	Typhoid	Negative	No sign of tuberculosis in history or examination; von Pirquet also negative.
64	Sept. 20, 1909	Martha T.	Cardiorenal	Negative	No sign of tuberculosis in history or exmination or autopsy; von Pirquet also negative.
65	Sept. 20, 1909	Dominic F.	Acute articular rheumatism	Negative	No sign of tuberculosis in history or examination; von Pirquet also negative.
66	Sept. 20, 1909	Anna T.	Typhoid	Negative	No sign of tuberculosis in history or examination; von Pirquet also negative.
67	Oct. 2, 1909	Sam. W.	Chronic endocarditis	Negative	No sign of tuberculosis in history or examination or autopsy; von Pirquet also negative.
73	Oct. 3, 1909	Joe F.	Acute bronchitis	Negative	No sign of tuberculosis in history or examination; simple acute attack; von Pirquet negative.
74	Dec. 20, 1909	Pasquale L.	Subacute bronchitis	Negative	No sign of tuberculosis in history or examination; von Pirquet also negative; malingerer (?)
77	Dec. 20, 1909	Sam. B.	Typhoid	Negative	No sign of tuberculosis in history or examination; von Pirquet also negative.
78	Dec. 20, 1909	Leminot B.	Lobar pneumonia	Negative	No sign of tuberculosis in history or examination; von Pirquet also negative.
79	Dec. 20, 1909	Thomas R.	Lobar pneumonia	Negative	No sign of tuberculosis in history or examination; von Pirquet also negative.
84	Oct. 5, 1909	Katie S.	Typhoid	Negative	No sign of tuberculosis in history or examination; von Pirquet also negative.
88	Oct. 15, 1909	Maggie O'L.	Acute articular rheumatism	Negative	No sign of tuberculosis in history or examination; von Pirquet positive.
89	Oct. 15, 1909	Maggie P.	Lobar pneumonia	Negative	No sign of tuberculosis in history or examination; von Pirquet positive; ordinary course, with crisis.
91	Oct. 20, 1909	Laura B.	Chronic nephritis	Negative	No sign of tuberculosis in history or examination; von Pirquet negative.
93	Sept. 29, 1909	Mary di M.	Congenital syphilis	Negative	No sign of tuberculosis in history or examination; von Pirquet negative.
94	Nov. 15, 1909	Mary O'D.	Acute bronchitis	Negative	No sign of tuberculosis in history or examination; simple acute case; von Pirquet negative.
95	Nov. 15, 1909	Mary L.	Lobar pneumonia	Negative	Ran ordinary course, with crisis; no sign of tuberculosis in history or examination.
98	Jan. 27, 1910	George F.	Typhoid	Negative	No sign of tuberculosis in history or examination; von Pirquet also negative.
99	Jan. 27, 1910	John H.	Bronchopneumonia	Negative	No sign of tuberculosis in history or examination; von Pirquet also negative.
102	Feb. 4, 1910	Pat. H.	Lobar pneumiona	Negative	No sign of tuberculosis in history or examination; ordinary case, with crisis; von Pirquet also negative.

TABLE 6.—(*Continued.*)

Case No.	Date of test.	Name.	Diagnosis.	Result.	Remarks.
103	Feb. 4, 1910	Sam P.	Toxic purpura	Negative	No sign of tuberculosis in history or examination.
104	Feb. 4, 1910	James S.	Lobar pneumonia	Negative	No sign of tuberculosis in history or examination.
110	Mar. 8, 1912	Jim F.	Chronic constipation	Negative	Very slight slough; no sign in lungs.
111	Mar. 9, 1912	Joseph S.	Acute bronchitis	Negative	Attack cured in three weeks.
117	May 11, 1912	Lily T.	Acute pleurisy	Negative	Cough; pain in chest; friction rubs; first attack; cured in two weeks.
119	June 1, 1912	Leah I.	Acute articular rheumatism	Negative	No sign of tuberculosis in history or examination.
122	Aug. 9, 1912	Frank C.	Acute traumatic pleurisy	Negative	Fell on side three weeks before; pain; cough; rubs all disappeared on second visit, three days later.
125	Aug. 30, 1912	Hyman R.	Debility	Negative	Weak, neurasthenic; no cough or signs in lungs.
133	Aug. 26, 1912	Joe L.	Acute pleurisy	Negative	Cough; pain; rubs in left chest; two days later nothing heard; six months later no sign in chest.
143	May 10, 1913	Bailey (P. G. H.)	Acute articular rheumatism	Negative	No sign of tuberculosis in history or examination.
144	May 10, 1913	Lane (P. G. H.)	Acute articular rheumatism	Negative	No sign of tuberculosis in history or examination.
145	May 10, 1913	Parker (P. G. H.)	Cardiorenal	Negative	No sign of tuberculosis in history or examination.
146	May 10, 1913	Hopkins (P. G. H.)	Senile dementia	Negative	No sign of tuberculosis in history or examination.
147	May 10, 1913	Simmes, (P. G. H.)	Acute gastritis	Negative	No sign of tuberculosis in history or examination.
148	May 20, 1913	Carl S.	Normal	Negative	No sign of tuberculosis in history or examination.
149	May 20, 1913	Edward K.	Normal	Positive (twice)	No sign of tuberculosis in history or examination.
150	June 17, 1913	Philip W.	Normal	Negative	No sign of tuberculosis in history or examination.

77 cases, 71 negative (21 von Pirquet negative); of these, one (No. 57) gave both a positive Moro and a positive von Pirquet; one (No. 149) twice gave a positive Moro; two (Nos. 88 and 89) gave negative Moros and positive von Pirquets; one (No. 35) a doubtful Moro, and one (No. 54) a negative Moro and doubtful von Pirquet.

Recently Chiaravallotti[9] has called attention to the importance of what he calls the "general reaction" following the administration of the cutaneous tuberculin test. He found in most cases of active tuberculosis a distinct rise in the leukocyte count, which he interpreted as a general anaphylactic reaction. For instance, in one case of undoubted tuberculosis he found the blood picture as follows;

	Red blood cells.	Hemoglobin.	Leukocytes.
2 P.M.	3,800,000	70 per cent.	17,200
6 P.M.	3,800,000	70 per cent.	16,000
9 A.M.	3,800,000	70 per cent.	15,800
After von Pirquet test:			
2 P.M.	3,600,000	70 per cent.	22,000
6 P.M.	3,600,000	70 per cent.	24,000
8 A.M.	3,800,000	70 per cent.	18,200

[9] Riforma Med. (Napoli), 1913, xxix, 94.

Though the intrinsic evidence in the above figures might cast some doubt on their value, we nevertheless determined to try out the value of this method. (See cases 135 to 141 in tables.) Owing to the exigencies of dispensary work, one count was made at the same time on successive days. A few cases sufficed to demonstrate its unreliability. In only 1 was the leukocyte count higher after the test than before; in 3 it was lower; and in 1 non-tuberculous case an equally great variation was found. In 3 advanced cases the total leukocyte count was so high (undoubtedly due to mixed infection) that a difference of 2000 and 3000, such as Chiaravallotti described, might easily be due to one of the several factors of error in the technique.

SUMMARY. 1. In 76 unselected non-tuberculous cases only 5 failed to give a negative reaction, and in only 2 of these was the Moro positive.

2. Of 24 cases in the first two grades of pulmonary tuberculosis all reacted positively, indicating as is generally accepted, the specificity of the reaction.

3. Of 10 cases of far-advanced pulmonary tuberculosis, 9 reacted negatively and 1 doubtfully positively.

4. Of 10 tuberculous cases other than pulmonary all reacted positively.

5. Of 28 clinically doubtful cases, by the Moro test 7 reacted positively, 6 doubtfully, and 15 negatively. In the 16 cases in which von Pirquet tests were also made, 9 negative Moro cases gave 7 positive and 2 doubtful von Pirquets, while 1 doubtful Moro gave a positive von Pirquet. The others tallied with the Moro tests.

CONCLUSIONS. 1. In the light of the above figures, reinforced by the opinions of others, we believe to be erroneous the prevalent opinion that positive reactions in adults are of little or no value.

2. The constantly positive reaction in all undoubted early and moderate cases of tuberculosis is a strong indication of the specificity of the reaction.

3. The negative reaction in 90 per cent. of the far-advanced cases indicates that after bodily resistance has been overcome, with the probable disappearance of antibodies, the tissues fail to react to the test.

4. As well as in pulmonary tuberculosis, the test is of value in the differential diagnosis of pleural effusions, joint diseases, abdominal tuberculosis *versus* typhoid, etc.

5. A general anaphylactic reaction, according to Chiaravallotti, as shown by an increase in the number of leukocytes in the peripheral blood following application of the test, is not demonstrable.

6. The test may be repeated on the same patient without alteration of the results. Although in our series the results were in every case the same, rare instances have occurred where repetition produced a different result.

THE SUCCESSFUL REMOVAL OF A TUMOR FROM THE FRONTAL REGION OF THE BRAIN.

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Although many cases of brain tumor operations have been reported, those in which the successful removal of a neoplasm has resulted in relief of symptoms are still few enough, it seems to us, to make a record of the following case worth while.

Our patient was first seen by Dr. Diller January 20, 1913, having been referred to him by Dr. Guy D. Engle. She was a married woman, aged fifty-three years, of good ancestry, the mother of four healthy children, and had previously enjoyed good health. The first symptom of her present illness occurred August 10, 1912. On this date while she was doing some work in the kitchen, the ring and little fingers of the left hand began to twitch; this twitching gradually extended to the entire hand, the wrist, forearm, and arm successively until the whole extremity was involved in violent convulsive movements which continued for nearly three hours; and at the same time there were twitching movements in the epigastric region. She was conscious throughout the attack. Since this attack the patient has had many similar ones, which at first occurred at intervals of a week or ten days, but recently have become more frequent, and now occur at the rate of about two in a week. These convulsive movements have always been strictly limited to the left arm, and have never involved any other part of the body except upon three occasions, when the epigastric spasms occurred similar to that described. The patient, however, states that for many years in her earlier life she had been subject to such seizures in the epigastric region, and that she had been quite free from them for many years preceding the first convulsion of her left arm. In one of the convulsive seizures (January 13, 1913) she was seen by Dr. Engle, the family physician, who observed that the movements were limited to the left arm and epigastric region. The most severe attack which she has had occurred about ten days before she came under our observation.

After the second arm convulsion the patient noted she could not wring clothes or sew so well as formerly—could not grip so tightly. The arm seemed to her to be growing increasingly numb and weak. About the same time she noted some numbness in the left leg, which had become marked in the previous two weeks;

with the development of this numbness she had noted increasing weakness in the left leg. The patient had never been unconscious in any of these convulsive seizures. She had had occasional attacks of vertigo, but had not been troubled with headache or vomiting, nor had her eyesight failed.

Examination. January 20, (Dr. Diller). The patient's mental condition was good. There was evident weakness of the left hand. Dyn: right, 55; left, 25. The left leg was weaker than its fellow. Pain, contact, and temperature sense in the left arm and leg were normal. Common objects placed in the left hand, such as a watch, bottle, etc., were recognized with a little less certainty and much less promptitude than by the right hand. Knee-jerks: right, normal; left, a little exaggerated. There was no Babinski reflex and no ankle clonus. There was no cranial nerve palsy and no nystagmus. The pupils reacted well to light and accommodation. The eye-grounds were perfectly normal. (Dr. Curry.)

Diagnosis. Here was a case of pure Jacksonian epilepsy involving the left upper extremity and abdomen, the attacks occurring with increasing frequency, and accompanied by a slow progressive paralysis of the left arm and leg and increased knee-jerks on the left side, but by no sensory changes. Headache, vomiting, and optic neuritis—all the major symptoms of brain tumor—were absent. Yet the symptoms pointed strongly to an organic lesion involving the cerebral cortex on the right side and probably irritating chiefly the arm centre. In view of the fact that the convulsive seizures were increasing in frequency and the patient was, especially of late, rapidly losing strength in the left arm and leg, she was advised to go to the hospital and submit to an operation.

She entered the hospital January 21, and was operated upon by Dr. Robert T. Miller, Jr., January 27. During this short period in the hospital, while awaiting operation, she developed no convulsive seizures; however, the weakness in the left arm grew much more pronounced, and at the time of the operation she was practically paralyzed in this member. The left leg had to a less extent also grown weaker.

Operation by Dr. Miller. First operation, January 27, 1913; osteoplastic craniotomy exposing the right motor cortex. Identification of a cortical tumor. Closure.

After etherization a rather large flap was outlined on the skin of the right side of the head corresponding to the underlying motor cortex and a tourniquet of heavy rubber tubing placed about the head. Upon exposure of the bone numerous perforations were made in the line of the incision with the Hudson drill, and by dividing the intervening bridges of bone with a Divilbiss forceps a bone flap was cut out whose undivided base was situated just above the pinna. The skull was extraordinarily thick and seemed unusually vascular, so that the cutting of the flap was a pro-

longed, tedious process and unavoidably attended by so great a loss of blood that even before the flap was turned back it became obvious that extended intracranial exploration was not feasible. Upon breaking up the bone flap the dura was found normal in appearance and under no recognizable tension; a corresponding dural flap was turned back. The exposed cortex seemed at first glance unaltered; the Rolandic fissure and the motor cortex were recognized, though no positive control of this observation was possible because of a lack of the means at hand to stimulate electrically. After a short search, however, there was found in the anterosuperior limit of the exposure a small area of cortex which was slightly paler and definitely softer than the adjoining tissue. In order to investigate this change the overlying edge of bone was rapidly cut out, whereupon it was found that this softened area lay just at the edge of a cortical neoplasm, and was evidently the result of compression. Upon further hurried exposure the tumor was found to be hard, slightly nodular, of a dark reddish-gray color, and sharply marked off from the adjoining cortex; it was situated just anterior to the upper portion of the motor cortex, and extended quite up to the midlongitudinal sulcus of the brain. The pia was densely adherent to the tumor, but the dura was quite free. At this stage of the operation the patient's condition rendered further progress impossible, and a hurried closure was made, with a few buried sutures in the fascia and a continuous silk suture in the skin, a small cigarette drain to the dura being necessary because of the oozing. The urgency of the patient's condition was evidently due to hemorrhage incident to the cutting of the bone flap; hence we hoped for prompt recuperation, and that, at a second operation, within a few days, it would be found possible to expose and remove the tumor—a hope which was fully borne out.

The patient made a prompt and uneventful postoperative recovery. There was only a slight amount of postoperative oozing, so that the drain was removed in forty-eight hours and the drainage tract closed tightly with two interrupted sutures in the skin in order to insure a clean field for the second operation. All sutures were removed on the fifth day. The patient's condition, after her recovery from the operative shock, seemed nowise altered, so that the second operation was undertaken on the seventh day.

Second operation, February 3, 1913. Enucleation of the cerebral tumor previously exposed. Closure.

Without previous cleaning the scalp was thoroughly painted with tincture of iodine, the osteoplastic flap turned back, and the cortex exposed and covered with a cotton compress saturated with warm normal salt solution; no anesthesia was needed up to this pont. The patient was now etherized and the overlying bone rapidly cut away until the tumor was completely exposed. It was necessary to carry the crainiectomy slightly past the midline at

one point. The tumor presented the same appearance as at the first exposure; its long axis was approximately 5.5 cm., running anteroposteriorly, and its width was about 3.5 cm. The situation of the tumor was just anterior to the extreme upper portion of the motor cortex, where it lay snugly tucked in between the falx cerebri and the right hemisphere of the brain. Attempt was now made to remove the mass by a slow dissection, with division of the cortical vessels between ligatures; but even a slight dislodgement resulted in so free a hemorrhage from the obscured region at the base of the tumor that this method had to be abruptly abandoned in favor of the more rapid enucleation with the finger. The tumor seemed well encapsulated and separated readily and cleanly from the brain tissue. As the falx was approached beneath the tumor the finger encountered slight though definite resistance, suggesting a pedicle attaching the mass to the deep edge of the falx near the corpus callosum. This suspicion was promptly confirmed, for simultaneously with the separation of this pedicle and the removal of the tumor the cavity was filled with the blood of a profuse venous hemorrhage. The bleeding was controlled by pressure, and after the field was cleared there was found at the deep edge of the falx a roughened lacerated area, from which the blood poured in a heavy stream. Evidently the pedicle was attached to the wall of the inferior longitudinal sinus, which had been torn during the process of enucleation. Difficult exposure and loss of blood ruled out any prolonged attempt to excise or suture this portion of the wall of the sinus. A small pledget of cotton, moistened in normal salt solution, was applied accurately to the rent in the sinus wall and held in place a few minutes, when, upon removal of the pressure, the cotton pledget alone was found to control the bleeding perfectly. A small cigarette drain was led to this pledget and the dura partially closed with a few interrupted sutures, the bone flap replaced, and the closure completed with a few interrupted sutures in the fascia and a continuous silk suture in the skin. The loss of blood during the operation of a little over an hour had been considerable, and the patient left the table in well-marked shock.

During the first eighteen hours after the operation the patient's condition was decidedly unpromising, with a pulse ranging from 120 to 160, and irregular at times; but after that she steadily improved, and subsequently passed through a satisfactory convalescence. The highest temperature was 101.4° eight hours after the operation, and for ten days there was a slight evening rise. The drain was removed on the fourth day and the skin approximated with sutures, as after the first operation. By the sixth day all sutures except those just mentioned were removed: the wound healed *per primam*, except for a minute opening in the anterior limb of the incision, from which there was a slight

drainage of clear cerebrospinal fluid for seven days. During the first five days the patient exhibited intermittently a mild delirium.

For the pathological report on the tumor, and the accompanying photograph we are indebted to Dr. A. T. Henrici, pathologist to St. Francis Hospital:

Macroscopic Description. The specimen consisted of a tumor mass measuring 4.5 x 3.5 x 3 cm. It was oval in outline and the surface was nodular. The tumor was everywhere covered by a smooth lining membrane, save on one side, where there was a small round depression having a roughened surface, indicating the point at which it had been detached from its pedicle. On section it is seen to be composed of small round masses the size of peas or larger, separated from each other by narrow bands of loose edematous stroma, which frequently showed hemorrhage. The tumor thus had a lobulated appearance. The tissue composing the lobules had a smooth, glistening white cut surface, showing occasional minute hemorrhages. It was moderately firm.

Photograph of tumor removed.

Microscopic Description. Sections of the tumor showed a vascular structure. Some areas were composed entirely of closely aggregated vessels and blood-spaces. Other areas had a more solid appearance, but on examining them with a higher power they were seen to be composed of similar closely aggregated capillaries, which had become collapsed, so that their lining cells had come into closer relationship with each other and gave the appearance of a solid tissue. Still other areas, which formed the greater part of the tumor, were composed of dense masses of cells compactly arranged. These cells were rather large, rounded, oval, or spindle-shaped cells, having large deeply staining nuclei and a rather indefinite, faintly staining protoplasm. Their nuclei occasionally showed mitotic figures, but these were by no means frequent. The cells showed no fibrils with phosphotungstic acid hemotoxylin. They were the same as the cells which lined the capillaries noted above. Occasional vessels were noted which had a well-defined muscular wall; but for the greater part the vessels existed as mere blood-sinuses, having no other lining than the tumor tissue itself. The tumor was supported by a rather small amount of dense connective tissue. In places heavy bands of stroma were noted.

Diagnosis. Hemangio-endothelioma of the dura.

COMMENTS (Dr. Diller): Following the second operation the patient was completely paralyzed in the left arm, face, and leg. Within a few days she regained power in her face. Three weeks later she began to get some strength in her leg; and after a period of six weeks some motion in the arm and shoulder returned. At this writing the patient is slowly gaining strength in both arms and legs. She is now able to walk without assistance. The arm is still weak, although gaining slowly and steadily.

This case is interesting from several points of view. Here was a growth of fair size which produced none of the well-known symptoms of brain tumor, but which manifested itself chiefly by Jacksonian epilepsy involving the left arm and by a slowly progressive hemiplegia. This tumor, situated just anterior to the right motor cortex, and lying between the falx and frontal lobe, would naturally be expected to produce symptoms referable to the trunk and leg rather than the arm. Yet from the onset there appeared to have been convulsions of the muscles of the upper abdominal wall accompanying those of the arm while the leg itself was never involved in convulsions. We were somewhat led astray in supposing the lesion chiefly located in the arm centre. The movements in the epigastric region we found difficult to interpret, since they occurred with only two or three of the arm convulsions; moreover, we had the patient's history that similar attacks had occurred over a period of many years running back to childhood. We were, therefore, disposed to eliminate these attacks from consideration as evidence pointing to localization of the lesion. Even now it is difficult to interpret them. If one considers these early epigastric convulsions indicative of a lesion in the frontal cortex involving the adjacent centre for the trunk there is great difficulty in explaining the long history, the disappearance of these convulsions for several years and their subsequent reappearance with the onset of trouble in the left arm. The patient also described these epigastric movements as definitely limited to that region of the body, and it was felt that this manifestation, whatever it indicated, was probably not related to the arm convulsions and hemiplegia.

From a practical point of view it will be seen that the old-fashioned trephining operation with an exposure of merely the middle Rolandic area would have failed to demonstrate the tumor; the value of a large osteoplastic flap is well illustrated.

This case also illustrates the practical point that a tumor may declare itself in an irregular and unusual manner. Besides the absence of general symptoms of brain tumor already referred to, the Babinski toe reflex and ankle-clonus, which one might expect to find, were both absent in this case. The knee-jerk, however, was distinctly increased, as compared with its fellow, and was a diagnostic sign of considerable value.

THE TOTAL NON-PROTEIN NITROGEN OF THE BLOOD IN PREGNANCY AND ECLAMPSIA.[1]

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and

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In the course of some recent work on the non-protein nitrogen ("rest" nitrogen) content of the blood in nephritis,[2] we had the opportunity to examine specimens from a number of patients suffering from eclampsia. As the results obtained in these few cases seemed to promise information of value, we collected additional material, and now present our findings in some twenty pregnant women, one-third of whom were normal while the remainder presented toxic phenomena of one sort or another. For the determination of the total non-protein nitrogen and urea of the blood we employed the technique recently perfected by Folin.[3] Only 5 or at the most 10 c.c. of blood are required, an amount readily obtained from a vein by a syringe. Strauss[4] has recently combined the method of collection and precipitation of the blood devised by Folin, with the ordinary Kjeldahl determination of the nitrogen, which may possibly be a fairly staisfactory procedure for the detection of gross variations when the special apparatus for the Folin method is not available. So far as we can ascertain no one has yet published a series of cases by the improved method we have employed, nor are data of any sort with reference to the nitrogen or urea of the blood in pregnancy available in any quantity.

Landsberg[5] examined the oxalated blood-plasma in a series of 18 pregnant women, clinically normal, and found, by the Kjeldahl method, the average content of "rest" nitrogen to be 24 mg. per 100 c.c. In 10 parturients the average was 23 mg., while in 8 normal non-pregnant women the average was 21 mg. per 100 c.c. In 1 case, however, in which the pregnancy was complicated by edema, albuminuria, and cylindruria the blood-plasma obtained

[1] Read before the Pathological Society of Philadelphia, October 9, 1913.

[2] C. B. Farr, and J. H. Austin, The Total Non-protein Nitrogen of the Blood in Nephritis and Allied Conditions, Jour. Exper. Med., 1913, xviii, 228.

[3] Newer Methods for the Determination of Total Non-protein Nitrogen. Urea, and Ammonia in the Blood, Jour. Biol. Chem., 1912, ii, 527.

[4] Zur Prognosenstellung bei Nephritis, Zeitsch. f. Urol., 1913, vii. 287.

[5] Utersuchungen ueber den Gehalt des Blutplasmas an Gesamteiweiss, Fibrinogen und Reststickstoff bei Schwangeren, Archiv. f. Gynak, 1910, lcii, 693.

ten days before delivery showed a content of 276 mg., a very considerable increase over normal.

Zangemeister[6] bases his figures on the 9 cases of eclampsia which he examined by a similar method, and found them to range between 15.7 and 44.3 mg., with an average of 25.8 mg. per 100 c.c. He determined the freezing-point of the plasma and reached the conclusion that, "As a rule 'rest' nitrogen is somewhat increased in eclampsia dependent upon the molecular concentration of the blood. There are single cases, however, in which this increase fails, even although the cases may have further convulsions. This increase should not be considered as a cause of eclampsia, but rather a secondary appearance, due to a lowered diuresis." In this connection it may be stated that Strauss has found no definite relation between the nitrogen content and the depression of the freezing-point.

Herter[7] in an article which does not give his actual figures or methods, states that in his study of the blood in six cases of eclampsia there was no increase in the percentage of urea. In a subsequent paper he[8] concluded that in cases of eclampsia without chronic nephritis the percentage of urea in the blood was almost regularly normal or only slightly increased in amount. When chronic nephritis existed the urea was apt to be high, and when this was the case a fatal outcome was to be expected.

In the following table we have classed our cases in four groups. Group A includes seven cases of normal pregnancy. The total non-protein nitrogen ranged from 21 to 31 mg. per 100 c.c., while the urea (or more precisely the ammonia-urea fraction) varied from 7 to 15 mg. per 100 c.c. of whole blood. These figures we consider perfectly normal, and this is confirmed by the other tabulated data, with the exception, perhaps, of the phenolsulphonephthalein test, to which we will refer subsequently.

Group B consists of three cases, in which the most prominent symptoms were referable to renal insufficiency; in one case valvular cardiac disease was added as a complicating factor. In each of these cases the pregnancy was interrupted on account of the increasing severity of the symptoms. In these cases the total non-protein nitrogen ranged from 34 to 52 mg. per 100 c.c. and the ammonia-urea fraction from 11 to 30 mg. per 100 c.c. of whole blood. The estimatioms were repeated in 2 of these cases during the puerperium; in 1 case a slight and in 1 case a considerable decrease was found. It will also be noticed that the decrease was practically all in the urea. In 1 case the history suggested chronic nephritis, and the urine contained albumin and casts when the patient left the hospital.

[6] Untersuchungen ueber die Blutbeschaffenheit und die Harnsecretion bei Eklampsie, Zeitsch. f. Geburtsch. u. Gynak., 1903, i, 385.

[7] The Pathology of Uremic Intoxications, Montreal Med. Jour., 1898, xxvii, 321.

[8] C. A. Herter, On Urea in some of Its Physiological and Pathological Relations, Johns Hopkins Hospital Reports, 1900, ix, 69.

GROUP A—CASES CLINICALLY NORMAL.

No.	Age	Para	Month of preg.	Nitrogen, mg. per 100 c.c.	Urea, mg. per 100 c.c	Phthalein			Blood pressure	Edema	Albumin	Casts
						1st hour	2d hour	total				
1	22	II	5th	20	6	..	..	..	120	none	none	none
2	27	II	9th	23	10	21	11	32	140	none	none	none
3	21	I	9th	25	8	25	3	38	125	none	trace	none
4	25	I	7th	27	14	..	..	..	125	none	none	none
5	27	IV	7th	30	13	..	..	..	130	slight	trace	none
6	16	I	9th	28	14	25	25	50	130	none	trace	none
7	19	I	8th	27	10	28	19	47	140	none	none	none

GROUP B—CASES WITH RENAL SYMPTOMS PREDOMINATING.

No.	Age	Para	Month of preg.	Nitrogen, mg. per 100 c.c.	Urea, mg. per 100 c.c	Phthalein			Blood pressure	Edema	Albumin	Casts
						1st hour	2d hour	total				
1	37	I	5th	33	16	15	9	24	175	Extreme	Heavy cloud	Hyaline granular
1	37	I	10 days after delivery	29	..	..	..	..	160	Slight	Trace	Occasionally
2	39	II	9th	52	30	20	15	35	204	Moderate	Light cloud	Hyaline granular
2	39	II	14 days after delivery	29	7	23	12	35	195	None	Trace	None
3	20	I	9th	35	11	19	15	34	165	Moderate	Heavy cloud	None

GROUP C—CASES WITH ECLAMPTIC CONVULSIONS.

No.	Age	Para	Month of preg.	Nitrogen, mg. per 100 c.c.	Urea, mg. per 100 c.c.	Phthalein			Blood pressure	Edema	Albumin	Casts	Notes
						1st hour	2d hour	total					
1	18	I	1 day post partum	25	11	32	20	52	160	none	Trace	None	
2	24	II	8th	37	25	..	..	20	195	Marked	Heavy cloud	Hyaline granular	Died
3	29	III	9th	40	27	0	0	0	210	Slight	Heavy cloud	Hyaline granular	Died
4	23	I	1 day post partum	46	30	35	20	55	162	Slight	Heavy cloud	Hyaline granular	
4	23	I	14 days post partum	35	14	..	..	..	140	None	Trace	None	
5	19	I	9th	54	..	20	3	23	165	Marked	Boiled solid	Granular	
5	19	I	11 days post partum	25	11	25	20	45	140	None	Light cloud	None	
6	30	I	7th	51	22	20	18	38	210	Slight	Light cloud	Granular	
7	29	I	6th	72	50	..	..	..	180	Marked	Light cloud	Granular	Died

GROUP D.

No.	Age	Para	Month of preg.	Nitrogen, mg. per 100 c.c.	Urea, mg. per 100 c.c.	Phthalein			Blood pressure	Edema	Albumin	Casts	Notes
						1st hour	2d hour	total					
1	24	II	3d	22	8	50	18	68	116	Slight	None	None	Salivated
2	32	II	8th	23	11	..	..	..	160	Slight	None	None	Headache Retinitis
3	30	III	8th	20	8	30	10	40	130	None	None	None	Chorea

Group C includes seven cases presenting convulsions as a prominent clinical symptom. The eclamptic seizures varied in number and severity. One case, the first in this group, after a normal delivery had a typical eclamptic convulsions further attacks were avoided by immediate treatment. In this instance the total non-protein nitrogen was within normal limits, 26 mg. In the other cases the figures ranged from 38 to 72 mg.; both patients represented by these extremes died, but several showing intermediate values recovered. Of the latter two were examined again after they had made clinical recoveries, and in each a considerable reduction in the nitrogen was found.

It will be noted that the other laboratory findings were in the most part confirmatory.

Group D comprises three dissimilar cases: one of uncontrollable vomiting during the third month of pregnancy; one of persistent headache, hemorrhagic retinitis, and high blood-pressure, without urinary changes; and one in which the pregnancy was interrupted at the eighth month on account of a chorea of increasing severity. In none of these cases was there any increase either in the nitrogen or in the urea, the former ranging from 21 to 24 mg. per 100 c.c. and the latter from 8 to 12 mg. per 100 c.c. of whole blood. In the first case the vomiting ceased after admission to the hospital, but marked salivation persisted for some time. In the second case the symptoms improved after rest in bed, and practically disappeared after delivery. In the third case the outcome was also satisfactory.

In 15 out of the 20 cases the functional efficiency of the kidneys was estimated by the phthalein test of Rowntree and Geraghty. In general there was a tendency to slightly subnormal values even in normal cases; in the pathological cases there was usually a correspondence between the nitrogen retention and the diminished phthalein excretion. In one case, however, the nitrogen fell rapidly, with clinical improvement, but there was no rise in the phthalein elimination. The amount of non-protein nitrogen retained is probably an index of the temporary degree of toxemia

(uremia literally), while the phthalein elimination is an index of the excretory efficiency of the kidneys. In our normal cases the two-hour elimination ranged from 32 to 50 per cent.; in the cases with renal symptoms, in Group B from 24 to 35 per cent.; and in the eclamptics from 0 to 52 per cent. In the last group the figures were far from consonant with the clinical symptoms—that is, if we suppose the latter to be due in any way to renal inadequacy.

Turning to the literature we find that Sondern and Harvey[9] in a series of 18 pregnant women, clinically normal, determined an excretion of phthalein of from 21 to 58 per cent. in two hours, with an average of 45 per cent.; 1 case with a true renal lesion having convulsions, eliminated 24 per cent; 1 case in which albumin and casts disappeared from the urine shortly after delivery eliminated 38 per cent. Goldsborough and Ainley in normal pregnant[10] women found the excretion to vary between 13 and 67 per cent, with an average of 47 per cent. In the puerperium the figures ranged from 48 to 76 per cent., with an average of 61 per cent. Both averages are below that of healthy non-pregnant individuals. Erne[11] in two normal pregnant women found 70 and 72 per cent. of the phthalein eliminated; in a case of eclampsia at the fourth month of pregnancy, two tests showed 62 and 70 per cent. respectively. A case of renal disease in a pregnant woman showed 42 and 44 per cent. on two examinations.

The blood-pressure in Groups B and C showed a definite increase above the normal in all cases; in no case was the systolic pressure less than 160 during the acute stage. In the remaining normal and miscellaneous cases the blood-pressure was 140 or less in all, with one exception already noted. The urinary changes were also strictly consistent with the clinical symptoms.

CONCLUSION. In normal pregnant women the total non-protein nitrogen does not usually exceed 30 mg. per 100 c.c. of whole blood. In general hospital cases without demonstrable renal lesions it may frequently reach 40 mg. or more. Slighter disturbances of function are therefore more clearly defined in the former class.

In all cases of pregnancy in which there was definite renal insufficiency or eclampsia, with one exception, there was always a slight and in most cases a considerable increase in the total non-protein nitrogen. The degree of retention was similar to that found in parenchymatous nephritis rather than the higher grade common in the interstitial variety. It bore no definite relation to the severity of the symptoms. In only one case did the figures reach

[9] The Phenolsulphonephthalein Test for Estimating Renal Function in Pregnancy, Bulletin of New York Lying-in Hospital, 1912, viii, 172.

[10] The Renal Activity in Pregnant and Puerperal Women as Revealed by the Phenosulphonephthalein Test, Jour. Amer. Med. Assoc., 1910, lv, 2058.

[11] Functionelle Nierenprufung mittels Phenolsulphonephthalein nach Rowntree und Geraghty, Münch. med. Woch., 1913. lx, 510.

a height which, according to Strauss,[12] would suggest a dubious prognosis. This patient died; another, with much less retention, also died.

The relatively normal elimination of phthalein in some cases of eclampsia and the markedly lowered excretion in some clinically normal cases will not permit us to draw any conclusions as to its real diagnostic or prognostic value from this brief series.

The presence of a rising blood-pressure, the condition of the urine as regards albumin and casts, and the clinical picture are severally more important than either of the newer methods we have employed. Further experience may modify this view, for Widal considers the examination of the blood of greater prognostic, if not diagnostic, value than the examination of the urine.

We are indebted to Dr. R. C. Norris for the privilege of studying in this connection several interesting cases at the Preston Retreat.

PROLAPSE OF THE OVARY: ITS RATIONAL MANAGEMENT.

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Any prolapse of the ovary, as a distinct, clearly defined, and well-recognized entity, is a morbid condition of a not uncommon occurrence. That this organ of the female sexual system can be so displaced must be apparent to all observing gynecologists.

The left ovary, experience teaches us, is more frequently so disordered. Thus, firmly connected with the uterus by the short, stout, fibrous ovario-uterine ligament, it must, by forces of necessity, in the normal movements of the body, be altered somewhat in its position in various directions; and situated normally on the posterior and upper surfaces of the broad ligament, it is also put in intimate association with the physiological position and condition of the rectum, namely: its distentions as a reservoir for fecal matter and a channel for its evacuation. The physiological movements of the human body in daily life necessarily imply many alterations in the posture of the pelvic viscera to a varying degree. The wise dispensation of nature that an ovary can materially change its position without any derangement of its sensation or function is one of the many provisions of our created organization.

A displacement of any of the internal genitalia of the human female is then a morbid entity only when these alterations in position are persistent and unalterable by natural efforts, and when

[12] Loc. cit.

they become the sources of pelvic discomfort and constitutional disturbances.

Any displacement of the internal genitalia may be primary or secondary. Primary, when this alteration has no antecedent pathological change; secondary, when such morbid variations do exist.

Primary displacements are usually traumatic in origin and precipitous in action; secondary, are slow and insidious in causation, and gradual in manifestation.

Without doubt some cases are congenital, occurring in the formative stages of genital development.

Most cases of ovarian prolapse are secondary, and are necessarily aggravated by individual, coexistent, or antecedent conditions. These pathological changes partake of various varieties and degrees.

In the consideration of uterine displacements we classify these causes into : (*a*) those attributable to an increased bulk and weight of the organ; (*b*) those resultant from some relaxation of the normal supports; (*c*) those dependent upon an increased abdominal pressure from above; (*d*) those arising from abnormal tractile forces from below. So with the ovary. Two or more of these causes may be operative in the same case.

It is unnecessary to enter further into the special causes, contributing to an increased bulk and weight of the ovary, or to the underlying conditions favoring some relaxation of support. There is always some elongation of the suspensory or the infundibuliform pelvic ligament in such cases.

In this consideration of the subject of ovarian prolapse, we desire to have our remarks referable only and distinctly attributable to conditions in which the ovary is the only offending organ, and not to cases associated with, or dependent upon, backward or downward dislocations of the uterus.

Backache and sensations of pelvic weight and heaviness are ordinarily present, especially at the periods of ovulation and menstruation, owing no doubt to an intrapelvic physiological turgescence of blood-supply at this time. More pronounced and characteristic symptoms are pain during defecation, continuing, it may be, for hours after unless the stools are free and soft. Sexual intercourse is always painful, for the reason that the ordinary completion of this act implies more or less contusion of this displaced and tender organ.

There is usually menorrhagia and dysmenorrhea also.

The anatomical fact that the right ovarian vein empties obliquely into the ascending vena cava, while the left ovarian vein has its outlet at right angles into the renal vein, is one of the reasons why the left-sided organ is more inclined to have an obstructed venous circulation, and becomes, in consequence, more often the seat of some pain, with many of its structural lesions.

There are varying degrees of prolapse. To be unmistakably noticed, the utmost displacement must be present, that is, the ovary lies at the bottom of Douglas's fossa.

Constitutional symptoms are such as are usually manifested in many female pelvic diseases. In the main, both local and general symptoms are dependent on the vicissitudes of female life, with its many changes of pelvic circulation of an active or passive kind.

The diagnosis is easy, yet it may be confounded with a retroflexed uterus, with an extra-uterine fibroid, situated on the posterior uterine wall, or with the presence of a chronic pelvic inflammatory exudate. A careful bimanual method of examination of the vagina and rectum makes clear the nature of the case. From the first condition, it can, if needed, be safely differentiated by the gentle insertion of a thoroughly sterilized, flexible, copper uterine sound, followed by rest; and, from the latter, by the careful history of the case, and by the continuance, if not the persistency, of the retro-uterine morbid mass, unaltered by taxis, with the patient in the knee-elbow posture.

A prolapsed ovary is at times a tender, pulsating body—the most disturbing cases.

The most important of all things, in a practical sense, consists in the complete and permanent rectification of the displaced ovary, a condition which, if neglected, surely will sooner or later lead to a general disarrangement.

In the first place strict attention must be given to obtaining daily by diet, and by medicine if necessary, a full, free, soft, easy evacuation of the intestinal tube—the most important sewe, of the human body. For the most part the salines or the sulpho-saline mineral waters answer this purpose well during the summer months.

Occasional small doses of calomel (gr. $\frac{1}{10}$ each), followed by phosphate of sodium or sal Rochelle or Pluto Water, or a laxative pill of podophyllin, belladonna, and nux vomica, also accomplish this end at any time. The following rule should be observed: To take an appropriate dose of either, at night on retiring, or early the following morning fasting, provided the requisite movement of the bowels has not been obtained the previous day.

The avoidance of constipation not only cleanses the system, but it aids digestion; it gives less work for the kidneys to do, in the way of systemic elimination; it clears the skin and it promotes mental and bodily activity. How many women have obtained thereby a complete relief from repeated attacks of a troublesome migraine, or a less pronounced septic invasion of the nervous system, because of the processes of auto-intoxication.

In the next place, make certain of the judicious adjustment of the patient's clothing about the waist, and largely its suspension from the shoulders. Corsets, in size, shape, weight, and personal fit,

are needful; certainly, more improvement in these particulars is obtainable today than in years past.

In fine, it should be impressed on the patient's mind that continued efforts on her part are ever to be made to reduce the intra-abdominal pressure from above upon the pelvic viscera and their circulation. In so doing we are instrumental and helpful in adding to woman's comfort and activity of body, as well as improving the posture, the ease, and the grace of her movements.

It has been my practice for years to direct such patients as are afflicted with an ovarian descent to assume the genupectoral position of the body, with the chest resting on the mattress of the bed (face turned of course to either side), while the pelvis is elevated to the utmost. There is no better time in the day for this duty than early in the morning after the alvine evacuation, and again in the evening before retiring. Each time should consume about twenty minutes. The patient should always avoid lying on the back; always rest in the recumbent position, on either side, somewhat semiprone.

Constitutional treatment by medicinal agents and hygienic measures are of course advantageous. Special indications arise because of anemia, debility, general nervousness, and insomnia. Prolapse of the ovary is usually detected in debilitated, sensitive, and neurasthenic conditions of the system. Always, then, endeavor to elevate the standard of the general health by all reasonable hygienic measures.

In most instances of ovarian prolapse there is more or less menstrual disorder. There is no amenorrhea, but there is some dysmenorrhea, and at times a serious menorrhagia. The menstrual flow often appears too frequently, is usually prolonged in time, as well as increased in quantity. No doubt in such cases some structural vascular lesion is induced in the endometrium, by virtue of the morbid changes in the ovary, requiring special treatment for its cure. Thus a curettement of the uterus may be done at the same sitting, preceding the abdominal section for an oöphorectomy.

There are no specifics for this affection. Naught, non-operative, can be done beyond the utilization of the aforementioned means, faithfully and skilfully employed and the use of general tonic and hygienic measures. Local means may be needed to keep the vaginal canal clean, the pelvic congestion reduced, and its circulation regulated.

Mechanical supports for ovarian prolapse, with or without any association of a backward uterine dislocation by the use of pessaries, are painful and harmful. Vaginal tampons, constructed of absorbent wool, soaked with the thymolated boro-alumino-glycerite, are better.

The latter are employed to the best advantage as follows: Not to exceed twice weekly, in the absence of the menstrual time, the

patient assumes the genupectoral posture, when gentle taxis is applied to readjust the ovary. With Sims' speculum retracting the perineum and the posterior vaginal wall the vaginal surfaces are cleaned with dry absorbent cotton, when an appropriate size and shape of wool tampon, saturated with thymolated boro-alumino-glycerite, is firmly packed into the posterior vaginal cul-de-sac, and there allowed to remain for two full days. A hot vaginal douche should follow its removal. The patient then experiences more or less comfort, from the reason that the downward movement of the displaced ovary is counteracted and mechanically supported by the wool; and the congestion is diminished by the hydrogogue action of the glycerite. Palliation may follow these procedures, so much so that further treatment may not be required.

But surgical treatment is clearly indicated in many cases because the above-mentioned means and measures properly and faithfully used, sometimes fail.

The operation of oöphorectomy may have to be done on account of some serious structural changes of the ovary If so, it should always be done by the abdominal route, never by the vaginal method, for the reason that it can be so done more intelligently and thoroughly and just as safely. In this connection it is well demonstrated that an abdominal section affords the best of all means of determining accurately what is the condition within the pelvic cavity, the degree of the morbid process present, and what should be done for its betterment.

Modern pelvic surgery for women has unquestionably been overdone. In no way has it been so much abused as in the removal of some of the pelvic organs, under the impression that permanently good results are thus to be obtained. Experience teaches, however, in many instances the falsity of this belief. When to sacrifice the ovary is a serious question. While it is true that the removal of one ovary does not cause menstrual cessation, nor induce sterility, nevertheless it behooves us always to be careful and conservative, and to sacrifice no organ or the part of any unless reasonably necessary. With this understanding it seems to me that it should be done only for otherwise incurable structural lesions.

The abdominal section is best done with the patient in the Trendelenburg posture. The offending organ is seized by the fingers of the left hand, lifted up from the Douglas's fossa, where it had fallen, into the line of the abdominal section, when its attachments and its circulating vessels can be judiciously managed.

A needle, armed with a loop of No. 2 catgut, is first passed through the upper border of the broad ligament, adjoining the uterine wall; and a second one through the same structure on the pelvic side of the dislocated ovary. Both are firmly tied. All intermediate structures, including of course the ovary, are exsected. The raw and bare surfaces remaining along these lines are stitched over

in a continuous suture and closed, to prevent bleeding and to restrain septic infection. No pain ought to supervene if the section is aseptically done.

This method of the application of the ligatures is better than with the Staffordshire knot; yes, superior in every particular, popular though the latter has been made. The Staffordshire knot implies the strangulation of an unnecessary amount of tissue; consequently, for several days following, the patient suffers needless pain.

In the making of an uncomplicated oöphorectomy the normal attachments of the diseased organ may be transfixed by a needle, armed by a loop of sterilized catgut, which, divided into two sections, may be interlocked and tied. The corresponding Fallopian tube, unless diseased, remains undisturbed.

It will be found at times that the displaced ovary is fixed and becomes irreducible, because of peritoneal adhesions, demanding then, of course, its complete extirpation. Some remnants of an old chronic pelvic peritonitis are frequently found in these cases, complicating and stubbornly resisting a complete oöphorectomy, so much so that it becomes difficult to ascertain how much of the same lies at the bottom of the patient's pelvic disease.

Before any abdominal section is commenced, conservative surgical procedures are in all cases to be entertained. A partial ovarian section, the puncturing of any distended cystic formations, may suffice. For a simple displacement, the ovary not being seriously diseased, no exsection is needed, for a suspension of the infundibuliform ligaments answers all purposes. At the time of the operation an opportunity is afforded for the best display of judgment and skill on the part of the gynecological surgeon. Of course, both ovaries are to be lifted up for inspection. Let the patient's interests always be first considered. Let her age, her social condition, her desire for future offspring, become the problems paramount for an individual solution.

There is no constant special anatomical or pathological entity always existing in these cases of ovarian prolapse, just as there are none in any forward, backward, or downward dislocations of the uterus.

Some ovaries are found comparatively healthy; some are congested or inflamed; some the seat of follicular formations; again, cystic degenerations or small abscesses may be detected. When this organ is elevated and brought into view the opportunity is also afforded to examine its appearance, determine the structural alterations within, and judiciously decide what course of action it is best to pursue. Always remove the diseased ovary entirely or in apart as indicated, but let the healthy organs remain.

All cases of ovarian prolapse are, as intimated, associated with no inconsiderable amount of constitutional depreciation of general

health. Hence, as prolapsed and tender ovaries are most pronounced in neurasthenic women, it follows that measures of a tonic and roborant kind are essential before and following any possible intervention of a surgical nature.

Whenever a complete oöphorectomy of one side is done, experiments on the lower animals (rabbits) and experiences in human females prove that the remaining healthy ovary may take on a renewed activity, so much so that in from a few months to a few years in younger women a compensatory hypertrophy of the opposite organ has recompensed for the loss.

In some of these cases, there unquestionably is a degree of distinct chronic ovaritis. The left-sided pain complained of is more continuous, persistent and severe than the right—a peculiarity no doubt attributable to the proximity of this left lateral organ to the rectum, with its scybalous masses of feces, and because of an increased congestion in the organ.

The *Faradic* electric current, judiciously administered, will be found of signal service. Its application should be derived from a very long wire, at least 1500 yards; a number 36, with a mild, smooth electric motive force, and with very rapid interruptions of the rheotome—the more rapid the better. Any increase thereof should be very slow and gradual.

The strength of this current should be regulated by the sensations of the patient; it should never be productive of any unpleasant sensations; better only barely perceptible to her. The best results follow a 15 to 20 minutes' seance.

Such an electric current is distinctly analgesic in its effects.

The *galvanic* current is adapted only to old, long-continued, chronic cases, which are probably associated with varied perioöphoritic morbid changes. Then, the positive pole, wrapped with moistened (salt water) cotton, is lodged within the posterior vaginal cul-de-sac, while to the negative pole is attached a flattened electrode, covered with gauze, thick in structure, wet with a potassium iodide solution, and placed over the lower abdominal surface.

The galvanic current, passed through the intermediate structures, between the two electrodes, so decomposes the potassium iodide solution, that it attracts the iodine to the positive pole, with a deposition of the alkali at the negative. In this way the alterative and resolvent influences of the iodine is promoted, perhaps better than from the use of larger quantities of the same medicament by the mouth.

It seems to me, beyond any peradventure of doubt, that electricity, in the various forms of the Faradic current and the galvanic, each scientifically employed, is a remedy of no mean power, in gynecological therapy.

There are no distinctive or fixed anatomical changes in painful or prolapsed ovaries. Most cases are noticed in neurasthenic women.

Therefore, it is by a restoration of the nervous tone of the system at large, by a roborant plan of treatment, with manifest improvement of the general health that these sensitive organs cease to be tender, although somewhat downwardly displaced. It is to better the local circulation of the blood, and to improve the nervous condition of the patient, factors largely responsible for the symptoms present, that we must direct our attention in all of our treatment, both general and local. So it is in the management of dislocations of the uterus.

I have introduced this question for two reasons: (1) it has been imperfectly dwelt upon by most authorities of gynecological literature, and (2) it is a disease of enough frequency and importance to entitle it to greater consideration on our part.

PRECOCIOUS DEVELOPMENT OF THE EXTERNAL GENITALS DUE TO HYPERNEPHROMA OF THE ADRENAL CORTEX.[1]

By Henry D. Jump, M.D.,

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and

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of Philadelphia.

The case which we present is one of those rare conditions of childhood; of unusual development of hair on the pubes and face with hypertrophy of the external genitals, without menstruation, which are apparently due to hypernephroma of one adrenal body. A similar case was presented in life at a meeting of the Philadelphia Pediatric Society in 1903 by Dr. D. J. M. Miller.[2] The girl died shortly afterward and the autopsy, done by Drs. C. Y. White and V. Nisbet,[3] showed the growth to be hypernephroma of the right adrenal. Since the presentation of that case there have been collected by Bullock and Sequira,[4] Guthrie and Emery,[5] and Glynn and Dun[6] sixteen other cases of the same type. The discussions by these authors have made this subject more clear, and have added much to the knowledge of this and allied conditions. The history of our case is as follows:

[1] Read before the Philadelphia Pediatric Society.
[2] Arch. Ped., 1903, p. 932.
[3] Trans. Philadelphia Ped. Soc., 1904-05, V, i.
[4] Trans. Path. Soc. London, 1905, lvi, 189.
[5] Clin. Soc. Trans., xl, 175.
[6] Liverpool Med. Chir. Jour., 1911, xxxi, 116

CASE.—G. M., aged seven years, schoolgirl. Father and mother were living and well. The father was large and strong, the mother was small, frail, and suffered from splanchnoptosis. One brother, two years older, was living, was rather frail, but without distinct disease. A twin sister, much smaller and of a very different temperament, was living and well. There was no family history of cardiac, renal, tubercular, or malignant disease.

The patient was the larger of the twins, weighing six pounds at birth, while the twin sister weighed four pounds. During the first summer, on bottle feeding, malnutrition, with marked emaciation and weakness, developed, and after protracted and ineffectual treatment she was taken to the seashore, where her weight increased from twelve to twenty pounds. When one year old she began to develop rapidly, and a growth of hair was noticed, first over the pubes, then in the arm-pits, then over the legs and trunk. This was attributed to the oil baths she had been receiving. The skin of the abdomen and legs was rough. She grew rapidly, and showed a surprising mental and physical development. As she began to talk it was noticed that her voice was much deeper than that of a child, and at the age of six or seven years a laryngoscopic examination showed a development of the larynx and vocal cords suggesting that of an adult man. The bass voice attracted the attention of her playmates, and as she was subjected to banter and jest, she became diffident with strangers. She proved an apt scholar, and consequently attained high grades in her school-work. She was affectionate, and preferred to play with dolls, but elected to bestow caresses rather than to receive them. Her physical development enabled her to be more than a match for her brother and sister. When three years old she would carry heavy chairs about the room with an ease that amazed her parents. Her strength was phenomenal for one of her years.

In June, 1909, when seven years old, she had chickenpox and in July, whooping cough. Previous to this time the skin of the face had been smooth and the complexion good. After this, it became coarse, red, and rough from acne, and a beard started to grow. The character of the skin of the face, and the acne and growth of hair closely resembled that so often observed in boys at puberty. There was no pigmentation of the skin. Five months later the growth of hair on the face resembled that to be found on a boy of seventeen or eighteen years. The arms and legs were muscular, and suggested a masculine development. She had never menstruated. The trunk and neck were strong and well-developed: the nipples were of the masculine type. On account of the rapid development and hirsuties, she was repeatedly examined by one of us (Jump) for affection of the adrenal glands. None was noticed, however, until about August or September, 1909, when a mass was observed (Beates) in the right hypochondriac region. This

mass grew rapidly and was painless, but in December the abdominal distention was so great that it interfered with respiration. Later a severe dyspnea developed, and on December 22, she was admitted to the Samaritan Hospital, under the care of Babcock. At this time a physical examination showed a well-developed child, fifty-three inches in height. The estimated weight was about ninety pounds. The face showed regular but not prominent features, somewhat masculine in type, with a rough, red skin, and boyish beard and moustache of a brownish color. The hair of the head was long, slightly curly, dark reddish brown in color, and of moderate coarseness. The pubic and axillary hair was coarse, almost black in color, and the growth equalled that of an adult. The growth of hair extended from the pubic region to the umbilicus, and there was not the sharp demarcation of the upper border of the pubic hair noticed in women. A stiff growth of brownish-black hair was present upon the legs, thighs, and arms, and upon the anterior surface of the chest. The abdomen was greatly distended, especially on the right side, by a dense, elastic mass, which extended from the costal border to the pelvis. Although it was tympanitic below, it was, apparently, over the underlying colon. There was a slight enlargement of the abdominal veins of the right side, a marked linea albicantes over the lower abdomen, thighs, pubes, and flanks. The left flank was somewhat distended and tympanitic. There was no increase in the splenic or hepatic dulness. The apex-beat was in the fifth interspace, and of normal strength. The heart action was rapid (pulse, 136), but there were no murmurs. The respiration was 48 and embarrassed; there were bronchial rales, also an occasional short, unproductive cough. There was no distinct enlargement of the inguinal, axillary, cervical, or supraclavicular lymph nodes. The patient perspired freely. The voice was of a deep bass, and the child talked with difficulty on account of the dyspnea. The labia were thick and large, and there was a large growth of hair on the pubes, and a remarkable development of the clitoris; this was about one inch in length, half an inch in diameter,

FIG. 1—G. M., aged seven years, showing developmentof male character.

and notched on the under surface, closely suggesting a hypospadic penis. Later, after opening the abdomen, it was found that a normal infantile uterus, with ovaries and Fallopian tubes, was present. There was no evidence of a testicle in the labia or elsewhere. An examination of the blood showed the following: Hemoglobin, 85 per cent.; erythrocytes, 4,590,000; leukocytes, 8600.

The urine was negative, except for the presence of a moderate amount of albumin and amorphous urates; the specific gravity was 1030.

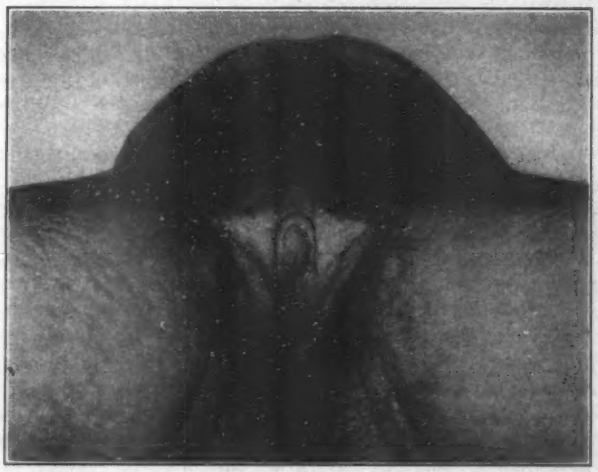

FIG. 2.—G. M., showing enlarged clitoris and growth of hair on genitalia.

The day after admission the child was etherized and a transverse incision was made over the right flank of the abdomen. This exposed an enormous perivascular and adherent hypernephroma, which was dislodged with difficulty, especially from its perivascular connections with the liver. During the operation, which lasted fifty minutes, the child became pulseless. After removing the growth the wound was closed, with drainage, and the patient stimulated, but although conscious and rational, she speedily sank, and died about three hours after the operation. The growth involved the whole of the right kidney. There was no line of separation between the adrenal and kidney. The sections which were made confirmed the diagnosis of hyprenephroma of the adrenal cortex. A limited postmortem examination was made. The left kidney and adrenal were normal. The uterus and ovaries were infantile. There were no metastatic growths found in the abdomen. The pituitary body was normal.

Counting the 17 cases collected by the writers cited above, this makes 18 of such cases reported in which the presence of hypernephroma of the adrenal cortex has been proved by autopsy. There have been other cases of this character reported without autopsy, and one reported by Guthrie and Emery in which the autopsy showed both adrenals normal. The report of this autopsy was brief and the examinations evidently superficial. Of the 18 reports, 14 were girls and 4 were boys. Among these cases there occurred an overgrowth of hair on the pubes in all, on the face in 14, and in the axilla in 5; overgrowth of the body due to the fat or muscular development in all; rough skin, with acne of the face, in some; menstruation and development of the breasts occurred in but one, that of Bullock and Sequiera; pigmentation of the skin was present in many, but there was in none a distinct bronzing of the skin, as in Addison's disease. Some of them showed a mental precocity, though the majority were probably mentally dull. There is a tendency to the development of the male at the expense of the female characteristics in the girls and an intensification of the male characteristics in the boys. The occurrence of a tumor of the adrenal cortex in all of the cases is more than a coincidence, and must be counted upon as the cause of the abnormal development. Tumors involving the adrenal medulla alone are not associated with precocious development.[7] That lesions of the adrenal cortex are associated with changes in sex characters may be shown by the following cases.

Thummin[8] reports a case of a girl, aged sixteen years and eight months, whose menstruation began at fifteen years and ceased when she was sixteen years. She then had a moustache and beard and hair on her thorax. She grew fat and her voice became masculine. Both adrenals were the seat of tumors, designated struma suprarenalis.

Hypoplasia of the adrenals has been found in cases of retarded development of the external genitalia and in reversion to the preadolescent stage. Weisel[9] reports a case of the former in a girl aged eighteen years. There were no hairs in the axilla and but few on the pubes; the breasts and external genitals were undeveloped.

Karakascheff[10] reports the case of a woman, aged thirty-nine years, mother of two children, who ceased to menstruate at twenty-seven years. There was scarcely any hair on the pubes and axilla. Both suprarenals were greatly atrophied.

Glynn[11] says that 15 per cent. of female pseudohermaphrodites showed a hyperplasia of the cortex in both adrenals.

[7] Glynn, Quarterly Jour. Med., 1911–12, No. V.
[8] Berli. klin. Woch., 1909, No. 3.
[9] Virchow's Archiv. 1904, clxxvi
[10] Beitrage v. Zeigler, 1904, xxxvi.
[11] Quarterly Jour. Med., 1911–12, No. V.

How to explain the relation of hypernephroma with these signs of precocious growth is not clear. Three hypotheses may be offered: (1) The adrenal cortex and the ovaries and testicles are derived from the same embryological tissue, the Wolffian ridge. It may be supposed that disturbances in the adrenal cortex may cause changes on the analogous tissues. As opposed to this, we have the fact that in but one of the eighteen cases (that of Bullock and Sequiera) was there a development of the ovaries. The presence of hirsuties of face and pubes which have no such embryological source cannot be explained in this way: (2) that the hypernephroma of the adrenal cortex has increased its internal secretion, and this has directly, or indirectly, in its effects on other organs affected the metabolism of the body in general and of the other parts affected in particular. These have been offered by Bullock and Sequiera and Glynn to explain the phenomena. We will venture a third based on the view of Sajous:[12] (1) That the pituitary body is connected with the adrenals by direct nerve paths; (2) that it thus governs, through the adrenals, general oxidation, metabolism and nutrition. The thyroid is also a part of this system. Lesions of the adrenal cortex may then cause such changes in the sympathetic systems as will produce these particular manifestations of overgrowth. In the case of Glynn and Dun the thyroid was markedly congested and gave the impression of overactivity; the pituitary was normal. In Bullock and Sequiera's case the thyroid and parathyroids were considerably enlarged; the pituitary was not examined. In the case of Guthrie and Emery the pituitary and other ductless glands were normal. In our case the pituitary was normal and the thyroid not examined.

Our interest in these cases must be more particularly along the clinical side, with the view of finding a method for the relief of the condition. There are three groups of precocious development which could be considered: (1) Those to which we have referred above, in which there is a development of the male characters and a lessening of the female characters, which seldom show true sexual precocity. (2) True sexual maturity in young girls, characterized by pubic and axillary hirsuties, enlargement of the breasts, and menstruation. These girls do not lose any of their female characters. They are due in some cases to a growth (cyst or sarcoma) in the ovaries.[13] (3) Early, true sexual development of boys. In some of these cases[14] there have been found tumor of the testicle, of the pineal gland, or of the adrenal cortex. In the second and third groups the removal of the growth has been successfully accomplished

[12] Internal Secretions, 4th edition, vol. i, p. 80.

[13] C. Lucas, quoted by Sequiera, Report of Society for the Study of Diseases of Children, 1902, vol. ii; Hofacker, Centralbl. f. Gynäkology, 1898, No. 41., Brohl, Centralbl. f. Gynäkology, 1897, No. 4.

[14] Sacchi, Riv. di Frimetria, 1895, xxi, quoted by Guthrie.

and in such there has been a reversion to the normal; the hair has fallen out, menstruation has ceased, and child-like qualities have returned. In Cushing's syndrome of overgrowth, with adiposity, due to pituitary disturbance, there is no overgrowth, of hair, and there are tardy or incomplete manifestations of the sex characters. These cases, then, need not be considered in the differential diagnosis of cause. Of the 18 cases which we have cited above, all died before they were sixteen years old. Some were operated on and died shortly afterward. In some the growth was inoperable. The symptoms of the three groups as detailed above are such as to make the diagnosis of these cases comparatively easy.

If, then, one meets a case of the first type, particularly if it be in a girl, there is presumptive evidence that there is a hypernephroma of the adrenal cortex. As there is 100 per cent. of mortality in these cases if let alone, exploratory operation, to determine if the adrenal is involved, seems advisable. If hypernephroma be found, its removal is indicated.

In considering operation on these children, we must bear in mind their apparent lack of resistance to surgical conditions. Adams's[15] case lived for seventeen months after an exploratory operation showed an inoperable condition. The others which were operated on succumbed soon after the operation. Even mild surgical procedures were sometimes fatal. Ritchie's case, four years old[16] died three days after an osteotomy, with no apparent cause except a slight infection of the wound. The case of O. Richards[17] died shortly after tapping for the removal of the ascites. In the case of Guthrie and Emery, which showed no change in the adrenals death followed soon after the opening of a large abscess in the groin. In all of these, however, the disease was well advanced. There is but one record of a case operated on early in life, that of Dobbertin[18]. This child, according to her parents, was born with a tumor in the abdomen, which at operation was the size of a fist. She died shortly after its removal. As a rule, children withstand surgical operations very well, and if the operation be done as soon as the condition is recognized the chance of success seems good enough to be used.

[15] Trans. Path. Soc. London, 1905, lvi.
[16] Cited by Bullock and Sequiera.
[17] Guy's Hosp. Rep., lix.
[18] Beiträge z. pathol. Anat., 1900, xxviii.

SYMPTOMS SUGGESTING PITUITARY DISORDER.[1]

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Remarks about the pituitary and other organs of internal secretion need preliminary explanations as to the writer's attitude. I realize the ease with which a group of systematized delusions may be built about the functions of the adrenal, thyroid, pituitary, or all of them together, but can see no evidence for a paranoid condition in the works of Cushing, Ashner, Biedl, and others where facts are presented and inferences drawn in a way which robs the skeptical and indifferent of the excuse that these affairs are too mysterious for the every-day work of the clinician. It has long been the proud boast of the general hospital pathologist that he knew nothing of the brain; a somewhat similar attitude is found in the psychiatrist's pride in being able to overlook all the confusing symptoms of internal secretory disorder, except that non-incriminating group found in Graves' disease.

Single cases of polyglandular and hypophyseal disease are reported in profusion. As best illustrated in Dr. Cushing's book, it is not hard to find descriptions of mental symptoms in a series of pituitary cases. I cannot, however, find pituitary symptoms described in a series of mental cases, or in a given population selected for their insanity, and this is the excuse for this paper, a survey which makes no pretence in intensive study of any particular case.

The problem of doing something to establish the frequency of pituitary symptoms in the Danvers population naturally divided itself into two parts, (1) the frequency of pituitary lesion in consecutive autopsies, and (2) the frequency of pituitary symptoms in the patients now in the hospital.

Approach to the first problem was easy. An autopsy index card was found which listed 45 lesions, 3 of them tumor with acromegaly; 4, tumor without acromegaly; 3, tumor secondary to other foci; and several instances of enlargement, cysts, marked adhesions, etc.

With the abundant evidence of the widespread results of certain lesions of the pituitary, it is worth noting that the pathologist had his attention called to obvious evidences of disease in 45 cases, or to 1 in 33 of 1600 consecutive insane patients—and this in routine autopsies from 1879 to 1912, where many glands escaped any sectioning for the microscope, and even those prepared for the microscope were removed and stained by a method which showed practically nothing of their functional ability, but allowed only a gross measure of a gross damage.

[1] Read at the March, 1913, meeting of the New England Society for Psychiatry, Howard, Rhode Island.

One of these cases was described by Dr. Worcester in 1896.[1] Another, clinically, was a picture of myxedema; autopsy disclosed a tumor filling the sella turcica. I give one other case to show a less definite symptom group: Last summer a married woman entered the hospital, emaciated, cyanotic, with a pulse that at one time was 174 to the minute, at other times 80, with glycosuria, silky infantile hair on scalp, eyebrows, and body, with clubbed fingers and thick, brittle nails, sluggish and irregular pupils, a slight increase in deep reflexes, and a negative Wassermann. Though the adrenal was supposed to be at fault, autopsy showed, beside adrenals with many cells missing, cystic ovary, atrophic breasts, a very large injected pituitary crowded with the nuclei of new cells.

To get some idea of the incidence of symptoms suggesting pituitary disease in the patients now in the hospital, wards were visited once with the physician in charge, about 950 patients coming in for a hasty observation, which was verified by a reference to the symptoms already recorded in the histories. Cushing's four groups of symptoms were kept in mind: (I) general pressure symptoms; (II) neighborhood symptoms, including visual and nasopharyngeal disturbances and uncinate epilepsy; (III) glandular manifestations, including skeletal over- and undergrowths, cutaneous and the important hair changes, adiposity, altered carbohydrate tolerance, polyuria, drowsiness, epilepsy again; (IV) symptoms referable to other ductless glands, including infantilism, pigmentation, persistent thymus. In this way ten cases were upturned whose symptoms, as recorded in the histories in the routine way, suggested a pituitary involvement.

Fig. 1.—Case II.

Case I.—A single woman, aged fifty-two years, who had scarlet fever at five years and had been feeble-minded since. She showed facial asymmetry; thyroid apparently diminished; poor hearing, poor vision, drowsiness, exophthalmos, a Wassermann positive on the serum, but negative on the cerebrospinal fluid; adiposity; height, 4 feet 10 inches; weight, 150 pounds.

Case II.—Married woman, aged forty-five years. At thirty years her eyesight began to fail, and at present she has cataracts

[1] Boston Med. and Surg. Jour., April 23, 1896.

which do not allow the condition beneath them to be estimated. At thirty-seven years, with the menopause, she began to get more fleshy, had frontal headache, which was much increased by noise, and severe bleeding from the nose. Height, 4 feet 10 inches; weight, 199 pounds. Her face was broad, nose short, vertex flattened; hands and fingers were short and thick; Wassermann was negative (Fig. 1).

CASE III.—Single woman, aged thirty-six years, who had meningitis at three and a half months, followed by hydrocephalus and feeble-mindedness. The circumference of head was 62½ cm.; height, 4 feet 8 inches; weight, 172 pounds; body square, covered with a deep fatty panniculus; arms short; Babinski present on both sides. The knee-jerks were very active. The patient was drowsy at times. She showed an irregular disk on both sides; veins dilated; arteries much smaller.

CASE IV.—Single woman, aged forty-one years. Imbecile, who as a girl had considerable headache and dizziness. Underdeveloped; overnourished; hydrocephalic; sluggish pupils; exophthalmos.

CASE V.—Girl, aged sixteen years. Height, 4 feet 9 inches. Weight, 100 pounds; fatty panniculus; hair fairly abundant; convergent strabismus; nystagmus. The left optic disk showed a nasal pallor.

CASE VI.—Married woman, aged twenty-three years. Always indifferent and feeble-minded. At nineteen years she had periods of stiffening, when she became cold, pale, with lips blue. Her height was 4 feet 7 inches; weight, 78 pounds on admission, and after typhoid at twenty-one years her weight was 98 pounds. In this patient was shown the body of a well-developed fat woman with the thin face and neck of a child.

CASE VII.—A man, aged fifty-one years. Since a fright at the Chelsea fire, when he was forty-six years, he has had many convulsions, preceded by a bad taste in his mouth. On entrance the skin of the forearms and abdomen was dry and scaly. Wassermann test was negative throughout; there was sugar in his urine for the first week. With a history of diminished taste for the last two years, there was an utter failure to pass the routine test for smell.

CASE VIII.—A widower, aged fifty-five years, who at twenty years received an injury to his back. At fifty-four years he was annoyed by falling to sleep at meals, in street cars, in conversation. Apparently normal mentally, he went to the Hot Springs to get relief from this condition, and in seven weeks was brought back violently insane. For some months, at the McLean Hospital, he was noisy, jocose, flighty, and distractible. This mental condition continued at the hospital, and he showed in addition a striking sexual complex full of symbolisms. His external genitals

approached the infantile type, and he had a tendency to a feminine distribution of hair. His height was 5 feet 7 inches. In the last year he had gained 22 pounds; weight, 229 pounds. He would fall asleep frequently, often in awkward positions. He was drowsy and manic by turns each day (Fig. 2).

FIG. 2.—Case VIII.

CASE IX.—A single woman, aged thirty-seven years, always feeble-minded. She was formerly considered pretty, but her face had changed. She was round-shouldered; the hands, femurs, and ears were of unusual length.

CASE X.—A single woman, aged twenty-three years; 5 feet tall; weight, 232 pounds, lack of axillary and pubic hair; infantile external genitalia.

Intensive study of these cases would probably remove some of them from consideration, but, on the other hand, applied to the whole hospital population, special methods would probably add many more cases to the list.

My point is this: State hospital populations, because of their long average residence, possibly because they are selected as insane, and because they do not in the first instance come to a surgeon seeking relief from the pressure symptoms, offer unusual opportunities for surveys of the incidence of pituitary symptoms to balance the intensive studies of the surgeon and experimentalist. For this more superficial work special methods of diagnosis are relatively unimportant; good routine physical examinations are wanted. Nothing better illustrates the value of the conscientious physical record than a glance at histories from a polyglandular viewpoint, and happily nothing so alleviates the tedium of what is often regarded as a useless task as the realization of interrelationships which give life and color to an otherwise bald and uninteresting statement of facts.

THE VALUE OF AUTO-INOCULATION IN PULMONARY TUBERCULOSIS.[1]

By Harry Lee Barnes, M.D.,

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Dr. Marcus Patterson, of Frimley, claims to influence the course of pulmonary tuberculosis favorably by "auto-inoculations" induced by labor. He states that even "severe" auto-inoculations, if controlled by immobilization, benefit the patients. He considers that "the aim should be to increase the patient's labor—insofar as is consistent with his physical capacity—in order to produce a marked deviation in the temperature on one or another of the grades, and finally enable him to do five hours hard outdoor work with little deviation." To collect evidence which shall help us to judge the value of such auto-inoculations is the object of this paper.

That graduated exercise has great value in attaining health and in preparing the body for athletic contests or work was well known to the ancients. Brehmer recommended exercise for consumptives. Walther prescribed graduated walking exercises for his patients for many years at Nordrach. Graduated labor as a therapeutic measure seems to have been first applied systematically to consumptives in sanatoria by Dr. Lawrence F. Flick. Great credit for elaboration of the system and popularizing it, for calling attention to the symptoms of slight "auto-inoculations," and the importance of treating them is due to Dr. Patterson.

[1] Read before the National Association for the Study and Prevention of Tuberculosis, Washington, D. C., May 8, 1913.

While unrecognized auto-inoculations may, of course, occur without rise of temperature or other symptoms, yet the most important single symptom of auto-inoculation and the one chiefly relied on for this study was a rise of temperature above 99°. Patterson considers even 99°, with headache, loss of appetite, or other marked constitutional symptoms, reliable evidence of auto-inoculation in men and 99.6° in women. Many tuberculous women are subject to a rise of a few tenths of a degree during menstruation, but at other times I have not found so marked a difference between men and women.

While it may be admitted that a temperature of 99° in some individuals does, and that 99.2° or even 99.4° in other individuals does not, usually mean tuberculous toxemia, yet it was considered the safest guide for this work.

Shortly after the opening of the institution it became our routine practice to interview patients with temperature over 99.5° and record the complications on the temperature charts. All complications causing fever were therefore eliminated with reasonable accuracy. The material at hand consisted of the records of 1517 patients discharged from the Rhode Island State Sanatorium during the years 1906 to 1911 inclusive. All far-advanced cases and all moderately advanced cases whose temperatures were not reduced absolutely to normal for periods of two or three weeks were eliminated. All tuberculin-treated patients, all children, and likewise all colored persons, have been excluded as not forming a fair basis of deduction. In the following table the remaining 746 patients have been classified according to the average frequency of the fever days in the left-hand column, and according to their present condition in the remaining columns. The majority of these auto-inoculations were between 99° and 99.6°, and for one or two consecutive days only, but a small minority had long runs of fever.

TABLE I.—End Results Classified According to the Average Frequency of Fever Days.

Average frequency of temperature.	Well.	Living and working.	Living.	Dead.	Totals.	Per cent. Dead.
3 times week	12	9	8	50	79	63
2 times week	30	20	25	69	114	47
Once in 1 week	62	39	30	74	205	36
" " 2 weeks	34	21	14	33	102	32
" " 3 weeks	22	16	14	14	66	21
" " 4 weeks	16	16	11	14	57	23
" " 2 months	12	9	6	5	32	15
" " 3 months	6	6	4	1	17	5
" " 6 months	10	..	2	..	12	0
Never	10	12	5	5	32	15
Totals	214	148	119	265	746	35

From the above table it appears that both the recovery and the mortality rate of tuberculous patients bear a pretty constant relation to the number of auto-inoculations as determined by the number of fever days. Everyone would expect that patients who had some fever with an average frequency of three, two, or even one day in a week would turn out badly. But if occasional auto-inoculations evidenced by slight fever are beneficial, should not those who have auto-inoculation on an average of one day in two, three, or four weeks do better than those who have them one day in two, three, or six months, or none at all?

The great majority of the 93 patients whose fever days averaged one day in two months or more of residence had only a slight initial fever for a few days after admission, so that they had no inoculations which would be considered of therapeutic value by Patterson, and yet these are the patients whose recovery best stood the test of time.

Our patients are kept in bed with a temperature of 100° or over if persistent, and for anything above 99° in the morning; but as we have not carried out the complete immobilization described by Patterson, it may be said that some of the patients not receiving this complete immobilization were injured by these auto-inoculations which otherwise might have benefited them. To ascertain whether lack of control of the immobilizations could have affected the result, and also to eliminate from consideration the worst types of cases, all patients whose temperatures were not always reduced to 99° or below in less than one week were excluded from the following tabulation:

TABLE II.—End Results Classified According to the Average Frequency of Fever Days. All Auto-inoculations Controlled in Less than a Week.

Frequency of fever.	Well.	Living and working.	Living.	Dead.	Total.	Per cent. Dead.
2 times week	3	3	2	6	14	42
Once in 1 week	20	14	9	17	60	28
" " 2 weeks	24	12	12	18	66	27
" " 3 weeks	17	13	11	14	55	25
" " 4 weeks	14	14	12	10	50	20
" " 2 months	13	9	6	6	34	14
" " 3 months	5	6	3	1	15	6
" " 6 months	9	0	2	0	11	0
Never	9	13	5	5	32	15
Totals	114	84	62	77	337	22

That the results in patients who had no reactions were not quite so good as those who averaged one auto-inoculation in six months, may fairly be explained by the fact that the former had an average residence of only 2.8 months against 6.5 months for the latter.

The principle that the fewer the fever reactions the more permanent the results is clearly seen in Table II, which also shows

that the poor results in those having auto-inoculations was not due to lack of prompt control.

All our patients had been on a system of graduated exercise and work about the institution since the fall of 1905. The system is similar to Dr. Patterson's except that there has been no so-called "complete immobilization" and no graduation of labor in foot pounds, and that in our application of graduated labor we have been trying to avoid instead of trying to induce temperature reactions. In order to be discharged "disease arrested," our classification requires that there must have been no hemoptysis, acute pleurisy, troublesome cough, nor fever temperature over 99° for at least two months, the weight, strength, etc., being restored to normal. Tubercle bacilli may or may not be present. The majority of our patients discharged with their disease arrested have been worked up to four or four and one-half hours labor, such as sweeping, scrubbing, and waiting on table, in addition to three or four hours' walking exercise, but a few have not done quite so much. In order to make a more searching inquiry as to the value of auto-inoculations under graduated labor, the records of 169 patients who were classified as "disease arrested" on discharge have been tabulated in two classes: (1) Those who were either afebrile throughout the entire period of sanatorium residence or whose slight fever subsided in a week or two after admission and afterward remained afebrile, and (2) those who had occasional auto-inoculations over a considerable period, but whose temperature finally settled absolutely to normal for over a month before discharge. In most cases this period of normal was at least six or eight weeks. Patterson's rule of ignoring an occasional rise of temperature in women provided it kept under 99.6° and was unaccompanied by constitutional symptoms was followed. A few who had a single rise to 99.5° or less were allowed in Class 1. No patients were admitted to Class 2 unless they had at least three auto-inoculations, and the majority had from three to six. Patients in Class 1 had their disease arrested without auto-inoculations, as indicated by fever, and those in Class 2 had their disease arrested after a period during which they had occasional auto-inoculations, as evidenced by fever.

The present condition of these patients is shown in the following table:

TABLE III.

	Well.	Living and working.	Living.	Dead.	Total.	Per cent. Dead.
Class 1, without auto-inoculations	28	18	10	9	65	13.8
Class 2, with auto-inoculations	39	31	13	21	104	20.2
Total	67	49	23	30	169	

While pulmonary tuberculosis is progressing favorably toward arrest, the value of graduated labor in restoring the normal muscular tone in working people, provided it can be done without inducing symptoms, can hardly be denied. There is some risk that fever reactions may be induced no matter how much we try to avoid them, but this risk must obviously be taken sometime if the patients' usefulness is ever to be restored. Graduated labor has value as a test for the patients' fitness to return to work, and also as a means of avoiding the injury to intellect and morals resulting from long continued idleness. However attractive the theory may be that fever reactions induced by labor have a curative value in pulmonary tuberculosis it cannot be accepted until proved by comparing the subsequent histories of patients who have had such reactions with similar patients who have not had them.

SUMMARY. 1. The fewer the fever days in pulmonary tuberculosis the better the chance of recovery.

2. Patients who have had no auto-inoculations evidenced by fever during sanatorium residence have a very high recovery rate.

3. Patients who finally achieve a stable temperature after a period of occasional auto-inoculations do not avoid relapse so successfully as those who obtain arrest without such period of auto-inoculations.

4. It should be our aim to avoid rather than to induce fever reactions, or auto-inoculations, in pulmonary tuberculosis.

THE EARLY SYMPTOMATOLOGY OF CANCER OF THE ESOPHAGUS.

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DURING the past two years the writer has had occasion to examine a considerable number of patients having cancer of the esophagus, and has been impressed with the difficulty which is experienced by the profession in recognizing the early symptoms of this disease. Aside from any practical reasons relative to a safe operative treatment of cancer of the esophagus, the mere desirability of knowing at the start the real condition of any patient should be sufficient reason for making an early diagnosis. In other words, to aim to make the earliest possible diagnosis of any pathological condition is but a part of the perfecting of medical science, and, even if the condition may be at present incurable, we should rather

feel the more stimulated to achieve its early recognition as the direct step toward the discovery of an ultimate cure.

At the present time, some of the problems connected with the successful removal of epithelioma of the esophagus have not been answered. We are, however, near their solution; how near is demonstrated by the fact that the resection of the esophagus has been shown to be technically possible upon man, and is already an easily accomplished proceedure upon the dog.[1] In the writer's opinion it is not too much to expect that at the present time the resection of the carcinomatous esophagus could be an accomplished fact upon the human being by the technique described by him[2] were opportunity offered to perform this operation under favorable conditions.

Every effort should, therefore, be exerted toward finding these patients in the earliest stages of their disease. By this is meant not only the necessity of employing some exact objectve method of diagnosis, but also the necessity of suspecting possible esophageal cancers in their incipiency.

With esophagoscopy we have at our command objective methods of arriving at an exact diagnosis. By these means, especially the latter, nothing can be simpler than the making of a correct diagnosis of esophageal affections once their presence is suspected. Not only can the presence of a cancer and its exact location be determined, but also by the removal of a small piece for microscopic examination the degree of malignancy. Furthermore, in case the growth is situated at the lower extremity of the esophagus it can be ascertained whether it orginated within the stomach or esophagus. This fact may not seem to be a matter of much clinical importance, but, if operative removal is considered, it becomes a consideration of much importance, for it furnishes a basis for estimating the probable size of the growth.

With, therefore, such an accurate method of diagnosis at our disposal, the early recognition of cancer of the esophagus resolves itself into a correct appreciation of its earliest symptoms. In other words, we have at hand means to make the diagnosis without error the hour the trouble is suspected, and the only bar to our actually doing so in an early stage is our difficulty in suspecting the trouble in its beginning.

The writer is convinced that the existence of cancer of the esophagus is suspected later than it should be, and that errors of diagnosis, even up to a late stage in the disease, are more frequent than it is generally supposed. Richard Cabot makes the statement in his recent paper upon diagnostic errors, among 3000 cases coming to autopsy, that a greater proportion of mistakes were made in the

[1] During the time in which this paper was in press, the reports of two cases of successful resection of cancer of the esophagus have been published.

[2] Annals of Surgery, July, 1910.

diagnosis of cancer of the esophagus than in any other condition. Out of 20 cases, 4 were missed altogether and 3 others merely suspected during life. He further states that the percentage of incorrect diagnoses would have been larger but for the routine use of the esophagoscope. He did not refer to cancer of the esophagus in the early stages, but to failures to recognize the true condition during life.

Cancer of esophagus, showing at (x) section across abscess cavity in lung and pleura.

The accompanying photograph represents a cancer of the esophagus which was diagnosed as empyema until the autopsy revealed the real cause of death. For this specimen I am indebted to Dr. Larkin, pathologist of the City Hospital. An early perforation of the growth had taken place, with an encapsulation of pus within the lung and adjacent pleura.

In my own experience the mistakes in the early diagnosis of those cases of cancer of the esophagus which have been submitted to me for an esophagoscopic diagnosis have not been very frequent.

Only 4 out of 21 cases have been suspected during the first two

months of symptoms. Rarely is a patient sent for esophagoscopic examination before four months from the date of his first symptoms, and several cases have not been examined until eight months to one year from the date of the first symptom. If cancer of the esophagus were a curable condition, such delay would be inexcusable. There is a general and well-recognized apathy toward the early recognition of cancer. Experience with cancer of the stomach where we have to deal with a lesion susceptible to radical removal, but where success is almost universally prevented by delayed diagnosis forces us to believe that the delay in the diagnosis of cancer of the esophagus is to be attributed in large part to indifference. Furthermore, cancer of the esophagus is a comparatively infrequent lesion. Probably not more than 1200 originate yearly in the United States; this figure is based upon the percentages of esophageal cancers to the total number of cancers. Not many physicians, therefore, see these cases. For this reason, there is a general ignorance concerning the early history and a general failure to recognize the necessity of applying absolute methods of diagnosis upon the appearance of the first symptoms. Whatever form of treatment may be applied to cancer, success cannot be hoped for unless an early diagnosis is made.

With, therefore, the yearly increase in our knowledge, resulting from research work upon intrathoracic conditions, it is not too much to hope that what has already been regularly accomplished upon animals, and what has been proved to be possible upon human beings, may yet be safely performed upon the latter—namely, the resection of the esophagus. In connection with any treatment, however, particularly in connection with the operative treatment, the question naturally suggests itself. How early may cancer of the esophagus be recognized if it is looked for upon the first appearance of symptoms? Autopsy statistics furnish strong evidence that it may be recognized when still of comparatively small size and limited to a short segment of the tube. At least 50 per cent. of the patients die without metastases.

These observations are further confirmed by the findings upon the operating table. The writer will limit himself entirely to his own experience. He has operated upon four patients with cancer of the thoracic portion of the esophagus. Although a radical operation was undertaken in only one of these cases, none of them was really inoperable. Enlarged glands were, however, present in all. The operation was undertaken in the four cases at four months, three months, eight months, and again, eight months from the date of the first symptom. The impression was very strong that had the patients been objectively examined in the beginning, favorable conditions for resection would have been found.

What, then, are the first symptoms of cancer of the esophagus? It is usually considered that dysphagia is the earliest symptom.

Such is often the case, but it is not generally appreciated that the dysphagia may be at first only temporary. This often has been the case among patients who have been referred to me. The dysphagia has entirely disappeared for a considerable length of time before it became permanent. In four of Cabot's 20 cases there was no dysphagia throughout the disease; I have not met with such a large proportion of strictly esophageal cancers in which dysphagia has been entirely lacking. An absence of dysphagia occurs more frequently in patients whose lesion has begun in the cardiac end of the stomach, involving the esophapus later. These patients have not been included in the present series. It is true, however, that dysphagia is long absent with true esophageal cancer. One patient during the first six months had three or four attacks of only a temporary dysphagia. In other patients the dysphagia at first may amount to a brief choking sensation only. It is not always the first symptom. Instead of it there may be some definite new abnormal sensations referable to the throat and interior of the thorax or region beneath the xiphoid cartilage. One patient referred to me complained of a sticking sensation in the throat and supposed that she had swallowed a tooth-brush bristle. An examination for such a cause of her trouble within the pharynx was actually made, and her physician assured her that there was nothing the matter. The patient still felt the disagreeable sensation, and returned after four months, with increased trouble. Six months after the beginning of her affliction the writer examined her and easily removed from her esophagus a small portion of a squamous-celled epithelioma for microscopic diagnosis. In other patients the new abnormal sensation may be described as a sense of pressure, or a dull, constantly recurring discomfort, or in still others, an actual pain. Patients complaining of such symptoms, which are possibly referable to the esophagus or stomach, should not be discharged as neurasthenics, but should be urged to have an esophagoscopic examination. The writer has not met with a large number of strictly esophageal cancers in which dysphagia has been entirely lacking; an absence of dysphagia occurs as already noted more frequently in patients whose lesion has begun in the cardiac end of the stomach, involving the esophagus later. These patients have not been included in the present series.

In other patients the first symptom has been a cough or increase in the amount of mucus in the throat; in others, anorexia has been the first symptom.

The accompanying table gives the first symptom of 21 patients whom the writer has recently examined, and of whom he has kept a more accurate record than in the early period of this study.

The table also gives the time after the development of the first symptom at which an attempt was made to settle the diagnosis definitely.

A review of the table makes it quite clear that an earlier diagnosis was easily possible in all of these patients. In most of them the true nature of the dysphagia was misunderstood, and in a small minority only was the diagnosis made before three to four months after the patient had symptoms. When we consider that the total duration of cancer of the esophagus is probably about two years, and that few patients live longer than twelve to fourteen months from the date of their first symptoms, a delay of three or four months means a delay of a considerable proportion of the total duration of the disease.

The writer, of course, realizes that even from well-informed quarters the question will be asked, "Of what use is an early diagnosis of cancer of the esophagus." The toleration of such a *laissez faire* attitude stultifies research and is equivalent to the denial of the possibility of any further therapeutic progress.

In conclusion then the purpose of this paper is to emphasize the obligation resting upon the profession to study more carefully the early symptomatology of cancer of the esophagus, and to urge the immediate objective examination of patients suffering from symptoms which may even remotely be referable to the esophagus.

No.	Patient.	First symptom.	Subsequent early symptoms.	Time intervening between appearance of symptom and the making of diagnosis.
1	Bu.	Pain beneath xiphoid.	Dysphagia began two weeks later.	3 months.
2	Do.	Attacks of temporary dysphagia.	Continuous dysphagia four months later.	9 months.
3	Flo.	Dysphagia.	Masked by symptoms of appendicitis. After the appendix was removed the esophageal cancer was discovered.	2 months.
4	Ab.	Dysphagia.		6 months.
5	Na.	Pain and dysphagia.	Severe pain.	2 months.
6	St.	Increase of mucus in throat; pain on left costal border.	Loss of strength; dysphagia six months later.	7 months.
7	We.	Sudden attacks of temporary dysphagia.	Several similar attacks during next nine months, then constant dysphagia.	11 months.
8	Lo.	Dysphagia.	Constant dysphagia and vomiting.	3 months.
9	Kr.	Dysphagia.		3 months.
10	Mey.	Dysphagia.	Constant vomiting after nine months.	6 months.
11	Me.	Tickling in thorat.	Frequent vomiting and dysphagia after four months.	6 months.
12	Ma.	Dysphagia.	Vomiting and increase of dysphagia.	6 months.
13	Se.	Dysphagia.		5 weeks.
14	Bl.	Dysphagia		3 months.
15	Sh.	Anorexia.	Dysphagia one month later.	2 months.
16	Ja.	Dysphagia and constant dull pain over lower end of sternum.		4 to 6 months.
17	Le.	Dysphagia.		3 months.
18	Su.	Dysphagia.		1 year.
19	W.	Tickling in throat.		6 months.
20	F.	Anorexia.	Dysphagia and pain.	7 months.
21	E.	Temporary dysphagia.	Constant dysphagia after two months.	7 months.

REVIEWS

ANATOMY AND PHYSIOLOGY. A TEXT-BOOK FOR NURSES. By JOHN F. LITTLE, M. D., Assistant Demonstrator of Anatomy, Jefferson Medical College. Pp. 483 with 149 engravings and 4 plates. Phila. and New York: Lea & Febiger, 1914.

THE present volume, one of the Nurses Text-book Series, is fully up to the standard of these popular and practical books. The author has taken the two great subjects of anatomy and physiology and has so carefully correlated them that the reader, while learning about the anatomy of the body, at the same time learns the function of that part; surely a most facile and interesting method of acquiring knowledge. The relation of these two great subjects has been well maintained though at times it seems as if too great stress had been laid upon anatomy, with the neglect of the equally important physiology. Certainly in considering the relative importance of the two subjects to nurses, it would be advisable to subordinate the question of what the body is, to what the body does. Excepting this criticism and criticism of some of the theories of physiology as expressed by the author, the remainder of the book is most praiseworthy. There is a careful condensation and clear expression of the subject matter, two extremely important and most difficult factors in the process of bringing large comprehensive subjects down to the level of the beginner who is to be taught only the bare elements of the subject.

Those who have to do with the training of nurses realize the inadequacy of many of the existing so-called nurses' text-books. They should be the first, therefore, to welcome a practical yet carefully and accurately prepared book such as this and will doubtless lend their enthusiastic support to the effort that is now being made to produce books that are suitable to the needs of the training school. J. H. M., JR.

BLOOD PRESSURE FROM THE CLINICAL STANDPOINT. By FRANCIS ASHLEY FAUGHT, M.D., Medico-Chirurgical College, Philadelphia. Pp. 281; illustrated. Philadelphia and London: W. B. Saunders & Co., 1913.

WRITTEN by a man who has devoted considerable time and study to the clinical aspects of blood pressure, this hand-book, an ampli-

fication of his pamphlet on the sphygmomanometer (published in 1909), presents a *resume* of the clinical and experimental work, which has developed so largely the usefulness and popularity of this test.

Except for Janeway's book on the "Clinical Study of Blood Pressure" (published in 1904), there has been no noteworthy addition in book form to the rapidly accumulating stock of knowledge on the subject of sphygmomanometry. The appearance, therefore, of such a book is timely, and it should prove useful. Following Janeway's method, the first part of the book, and in the reviewer's opinion the better part, deals chiefly with the mechanical and physiological principles of sphygmomanometry. In the latter part an attempt is made to consider from the clinical viewpoint of etiology, pathology, diagnosis and treatment, the different diseases in which a knowledge of the blood pressure is of importance. Its small size necessarily precludes thorough consideration of all these branches. It would seem better either to have encroached on the field of medical text-books with a larger book or to have restricted the discussion to those features directly concerned with blood pressure. Chapter two includes an interesting historical review with a description of the different types of sphygmomanometers invented. It is a pity that although the author's two instruments are described and illustrated in some detail, the Nicholson adaptation, considered by many to be the best on the market, is not even mentioned.

It is also regrettable that in a book on such a timely and interesting subject so many misprints and errors of spelling, punctuation, and grammar should be found. For instance, on page 17 is found "bacterial" for arterial; page 114, "subtil" for subtle; page 134, "mellitis" for mellitus; page 141, "phenomiæ" for phenomena, and "grandular" twice for granular; page 162, "antidates" for antedates; page 163, "percordial" for precordial; page 232, "nitrate" for nitrite. Clearness might be helped in many places by a more liberal use of commas, also by properly punctuating the end of a quotation (page 91).

Numerous footnote references throughout the book afford ready access to the original authorities. Again, however, the form is open to criticism. Instead of following the regular method of giving year, volume, and page, one or other of these items is nearly always omitted and in some important citations the reference is not given at all (page 124). The matter dealt with at the head of page 221 is the same and in the same words as on page 62.

Paper, illustrations, and type are all satisfactory, though the headings are occasionally not typed consistently (*e. g.* Graupner's and Shapiro's test, page 164; "Other Infections," page 109, etc.

The presentation of facts is for the most part excellent. The last two chapters on methods of controlling blood pressure should

prove especially useful. One might take exception however, to the statement that "strophanthus has proved unreliable and should not be used" in the treatment of myocardial degeneration (page 166). Still more strenuously do we disagree with the opinion that "thus far no accurate means of measuring the several factors (of the heart's function, *i. e.*, rhythmicity, irritability, conductivity, etc.) has yet been found." Instead of thinking that "the many methods which have been suggested from time to time, all fall short of any great degree of accuracy," we hold that the increased scientific accuracy in measuring many of these very factors has led to the greatest advance in our knowledge of heart disease for at least the past quarter century. E. B. K.

HYGIENE OF SANITATION. A TEXT-BOOK FOR NURSES. By GEORGE M. PRICE, M. D. Pp. 236. Philadelphia: Lea & Febiger, 1913.

THE author states in his preface that this book is an attempt to give to the nurse a knowledge of the elements of hygiene in its various branches. He might well have made this statement more comprehensive, for the book, written in elementary manner, could be readily comprehended by the layman and read with much profit. It contains masses of information that could be used every day by those interested in the proper hygiene of the home, of the person, of the school, of the food supply, or of the various occupations. The author has made the apparent scope of his book too small; he might well have broadened it and dedicated the book to the general public. It is one of the few text-books intended for nurses that adequately meets the requirements and should prove a welcome aid to those in charge of the instruction of nurses.

J. H. M., JR.

THE PRACTITIONER'S ENCYCLOPEDIA OF MEDICINE AND SURGERY IN ALL THEIR BRANCHES. By J. KEOGH MURPHY, M.C. (Cantab.), F.R.C.S. Pp. 1423; London: Henry Frowde, Oxford University Press.

AN encyclopedia of this kind, coming as it does between the brief medical and surgical summaries on the one hand and the systems of medicine and surgery on the other, is well conceived.

It is surprising that in the comparatively brief compass of some 1400 pages such a multitude of subjects has been so satisfactorily covered.

It is presented as a book for the general practitioner who in his work is called upon to give advice in conditions which, in the course of years, will cover the whole domain of medicine and surgery. For the physician whose lot falls away from the medical centres this book will prove an especial boon and will in part compensate him for the lack of broadening and stimulating influence of the general and special medical societies, with their ready access to medical libraries and current medical literature.

The division of the matter into the main headings of medicine, surgery, eye, ear, nose, throat, and skin, is a natural one and much more acceptable for general and special reading than the oft used alphabetical arrangement.

As an actual working tool, in the hands of a practioner who has no further access to medical knowledge, it has suffered from the necessary condensation imposed on the writers.

As a general medical educator, this book should prove invaluable in the hands of those who might otherwise fail to keep abreast of the landmarks in medical progress. It also offers to the practitioner an opportunity to keep his general knowledge in a well rounded form. A. A. H.

WHAT HEART PATIENTS SHOULD KNOW AND DO. By JAMES HENRY HONAN, M.D., Special Lecturer on Cardio-vascular Disease in the Univ. of Georgia, etc.; pp. 204. New York: Dodd, Mead & Co., 1913.

THE object of this book, in the words of the author's preface, is to give encouragement and hope to those who know they have heart trouble, to urge those who are suspicious of its presence, to seek advice in time; to help, if possible, both these classes of persons to make the most of their lives with the limitations which deviation from the normal imposes. To this end the first half of volume, and to the reviewer's mind much the more valuable half, is devoted to hygienic considerations, adapted especially to heart patients, under such capitals as relaxation, clothing, exercise, diet, sleep, etc. In the latter half, having presumably obtained the interest of the reader, the dryer and more technical anatomical and pathological details are considered. Emphasis is laid throughout on the fact that "this book is in no sense to be a substitute for the physician, nor a promise of health to all who read its pages."

The advisability of offering such a book to the lay public is in itself open to criticism.

Given the need for such advice in printed form, the recommendations are excellent.

Objection might be taken to a few details: the laity do not gener-

ally believe that a valvular defect is always fatal (p. 158); it is misleading to call angina pectoris an affection of the arteries, so "that we may have anginal pains in any part of the body (p. 171). Between forty-five and sixty years of age is rather high for the average incidence of the disease. It is rather sweeping to say that "when a child is attacked by rheumatism the heart is almost invariably involved," p. 184). Such small points, however, hardly detract from the excellent presentation in a popular way of a difficult subject. E. B. K.

THE ELEMENTS OF BACTERIOLOGICAL TECHNIC. A LABORATORY GUIDE FOR MEDICAL, DENTAL, AND TECHNICAL STUDENTS. By J. W. H. EYRE, M.D., M.S., F.R.S., (Edin.) Director of the Bacteriological Department of Guy's Hospital, London, and Lecturer on Bacteriology in the Medical and Dental Schools. Second edition: pp. 518; 219 illustrations. Philadelphia: W. B. Saunders Company, 1913.

THIS new edition of Dr. Eyre's well known and exceedingly valuable book on techinc was occasioned by the growth of literature in recent years. The plan of the work is essentially the same as in the first edition. It can be used as a desk book by the student or individual worker, or as a guide for a teacher in laying out a course in practical bacteriology. The first part of the book is devoted to describing the behavior of the laboratory worker and familiarizing him with the surroundings and apparatus. Then follows a short description of the biological status of microörganisms, which is succeeded by an account of the manufacture of the media upon which they are grown. In natural sequence then are given methods of isolation, cultivation, identification, and inoculation of microorganisms. The eighteenth chapter is devoted to the study of experimental infection during life with which is included serology applicable also to natural human infections. The blood picture and temperature of experimental animals are given. Post mortem material is discussed next. A chapter is devoted to the special consideration of pathogenic bacteria. The final chapter and the appendix are among the most important and useful sections of the book. The former contains methods for the examinations of water, soil, foods, sewage, air, and disinfectants, including detailed lists of the necessary paraphernalia; while the appendix gives tables for weights and measures, computing thermometric scales, preparing dilutions, estimating pressure, and the use of antiformin.

The book is well arranged, and the cuts are all clear and instructive. H. F.

A Manual of Surgery. For Students and Physicians. By Francis T. Stewart M.D., Prof. of Clinical Surgery, Jefferson Medical College; Surgeon to the Germantown Hospital; Out-Patient Surgeon to the Pennsylvania Hospital. Third edition; pp. 742; 571 illustrations. Philadelphia: P. Blakiston's Son & Co., 1913.

Previous editions of this book have received notice in these columns. It is intended for the undergraduate and the medical practitioner "seeking a guide to present-day surgery" and is admirably adapted to the purpose. The fact that a third edition is called for so soon after the second is good evidence of its excellence.

In the present edition, important additions have been made to many sections as demanded by the growth of surgical knowledge and experience. Under anesthesia, Crile's work on anoci-association receives mention. In syphilis, the reader is kept abreast of the most recent advances in diagnosis and treatment. So also in the chapters on surgical technic, the vascular system, the lymphatics, diaphragmatic hernia, fractures, the brain, the spinal cord, and amputations—as noted in the preface.

The author's large clinical and teaching experience have given him exceptional facilities for producing a book of this kind and keeping it a leader in its class. E. B. H.

Practical Bacteriology, Microbiology, and Serum Therapy (Medical and Veterinary). A Text-book for Laboratory Use. By Dr. A. Besson, formerly Director of the Bacteriological Laboratories of the Military Hospitals of France. Translated and adapted from the fifth French edition by H. J. Hutchens, D.S.O.; M.A.; M.R.C.S.; L.R.C.P.; D.P.H. (Ox.). Heath Professor of Comparative Pathology and Bacteriology of the University of Durham, Englnd. Pp. 892; 416 illustrations. London: Longmans, Green & Co., 1913.

The appearance of the revised edition of Dr. Besson's book in English will be welcomed by all bacteriologists who are familiar with the previous editions in French. The work is intended as a guide for the student and the more experienced worker in the detection and identification of pathogenic microörganisms. The translator has not only translated the French text but has added such material as he considered necessary or that has appeared since the French edition was issued. Dr. Hutchens' has been free in his translation and has acheived a most pleasing and fluent style, rather rare in scientific books. In former editions all theoretical matter was omitted but this issue contains a short chapter

upon the subject of immunity and the properties of immune serums, dealt with in an applied manner. The first quarter of the text is devoted to a full consideration of laboratory technique, of which the chapters upon the microscope and animal inoculation are especially good. The second part is devoted to the bacteria proper which are presented in groups according to their most pronounced characters, as for example the nonspore-bearing, Gram-negative, non liquefying rods, or the Gram-positive or Gram-negative cocci. The various organisms are described under the headings experimental inoculation, morphology, biological characters and detection. It would seem that too little space is given to the cultural characters in a book intended to be a laboratory guide. Much attention is given to the serum tests and the uses of antisera. An apparent slip is noted in the discussion of the Pneumococcus, where it is stated that this coccus does not ferment inulin, thus differing from the streptococci. The reverse is what is usually accepted. The next section is given to the higher bacteria and the description is fuller than is commonly found. The author uses the generic name Discomyces for the Streptothrix. an adoption not yet widely made in this country. The spirochætæ are discussed in the next section with the full details of their cultivation. The fifth division of the book covers the protozoa, emphasizing the comparative pathology and describing the metamorphoses of the individuals. The filterable viruses and the examination of water, sewage, and air are given in the sixth and seventh sections.

The book is a most excellent one and is the more welcome since nothing of the kind exists in English. The authors have presented all the acceptable techniques in a very practical manner. The recommending of certain ones, a characteristic of Besson's work, is admirable. It is to be regretted that the price is so high, for this may prevent the book from getting into the hands of students who would greatly profit by it. H. F.

DORLAND'S AMERICAN ILLUSTRATED MEDICAL DICTIONARY. Edited by W. A. NEWMAN DORLAND, A.M., M.D. Seventh edition. Pp. 1107. Illustrated. Philadelphia and London: W. B. Saunders Company, 1913.

THE seventh volume of this up-to-date medical dictionary is not only up to the standard of its predecessors, but surpasses it. It contains several thousand more terms than the previous edition, and in addition there will be found a number of tables of tests, stains, and staining methods, methods of treatment, etc., all of

which should prove of value. A considerable amount of collateral descriptive matter has been included under the different headings, for example, under each drug are given its composition, sources, dose, etc., and a description of the structure of the different organs is given along with their function. The illustrations are excellent, and numerous, and the book as a whole deserves great commendation. S. S.

HANDBOOK OF PHYSIOLOGY. By W. D. HALLIBURTON, M.D., LL.D., F.R.C.P., F.R.S., Professor of Physiology, Kings College, London. Eleventh edition (being twenty-fourth edition of Kirkes' *Physiology*). Philadelphia: P. Blakiston's Son & Co.

THIS text-book is familiar to every teacher of physiology and thousands of students have obtained their fundamentals of physiology therefrom. Although thoroughly revised the bulk of the volume has not been increased, there being less than nine hundred pages of text. There is still a large demand for a book of this size, but the tendency recently has been to use text-books that contain much more subject matter, at least in the larger medical schools. Certainly more and more importance is assigned to the subject each year, and in this respect the book at hand does not follow the tendencies of the times. Nevertheless, the book has value, indeed great value, particularly to the student who wishes to review the subject on the eve of an examination, and to the busy practitioner who desires to look up, in the shortest possible time, a physiological point long since forgotten; for the book is splendidily arranged and carefully indexed. If he is satisfied with a rather superficial knowledge of the newer things being done in this subject, the volume is equally valuable and accurate.

In this edition the structure work is but little altered, nor is this necessary, for no book is more logical, or the descriptive material more lucid. Inevitably, however, new material must be introduced in a new edition of any work upon this subject, no matter how short the interval after the preceding one. And so here, the writer, has found this necessary, and revision has been undertaken not only in the right direction but also conservatively. Great changes are seen in the respiratory system, some in the chapter on circulation, and the chapter on reproduction is a new one. Nor have the chapters on digestion, kidneys, and special senses been neglected. Yet all this has been accomplished without increasing the size of the book, we see here how wonderfully conservative the writer has been. E. L.

SURGICAL EXPERIENCE IN SOUTH AFRICA, 1899–1900. By G. H. MAKINS, C.B., F.R., C.S.: Senior Surgeon to St. Thomas's Hospital, London; Vice-President of the Royal College of Surgeons of England, etc. Second edition; pp. 504, 28 plates; 105 illustrations: Oxford University Press: 1913.

THIS, the second edition, is practically a reprint of the first, except for the continuation of a few of the histories, and was gotten out because of the continued demand for the work.

The work is merely a recounting of a wonderful series of cases, chiefly of the bullet wound variety, in the personal experience of the author.

In the introduction is given an excellent description of the various bullets and rifles, their peculiarities of trajectory, penetration, vulneration and fatality in reference to their relative size and composition.

The author discusses in minute detail the affect of bullets, immediate and remote, in all parts of the body, the incidence of the great number of aseptic wounds, and their ultimate behavior if infection does occur. The advantage of the small caliber high velocity projectile to the person hit is conclusively shown by comparison with wounds from the older style rifle balls.

Wounds of the soft parts, bones, joints, nerves, vessels, head, spine, and abdomen are all given ample space for consideration and description. The chapters given up to vessel injuries are exceedingly interesting, especially the data concerning aneurysms and arteriovenous communications. The text dealing with bone injuries is richly supplied with a large number of very excellent reproductions of x-ray photographs.

The book is not intended for a text-book in any sense of the word, but merely a relation of a series of interesting and instructive facts gleaned from a very unusual personal experience of the writer. It is most instructive and affords interest to the reader throughout. E. L. E.

SKIN DISEASES IN GENERAL PRACTICE. By HALDIN DAVIS, Physician in charge of the Skin Department, Paddington Green Children's Hospital; Chief Assistant in the Skin Department, St. Bartholomew's Hospital; Assistant Physician to the Hospital for Diseases of the Skin, Blackfriars. Pp. 340; 62 illustrations. London: Henry Frowde; Hodder & Stoughton, 1913.

THE writer has classified diseases of the skin, in so far as possible, upon a typographical basis. He has arranged the subject in the following divisions: Introduction, including a cursory review

of the pathology; disease due to the common pyogenic organisms; eczema; syphilis; diseases giving rise to wide spread eruptions; eruptions affecting the face; eruptions affecting the limbs; diseases affecting the hands and feet; diseases of the nails; diseases with lesions on the pudenda and in the groins; diseases limited in extent but irregular in distribution; bullous eruptions; anomalies of pigmentation; diseases of the scalp: modern methods of treatment. Only the common diseases of the skin are included in the work. There is naturally a considerable amount of repetition, as some of the general diseases are also mentioned under the restricted regional divisions. The book contains seven excellent color photographs. A few of the black and white pictures are rather poor.

F. C. K.

AIDS TO GYNECOLOGY. By S. JERVOIS AARONS, M.D. (Edin.), M.R.C.P. (Lond.), Gynerologist to St. Anthony's Hospital, etc. Fifth edition; pp. 124; 4 illustrations. New York: William Wood & Company, 1913.

THE present volume which has reached its fifth edition contains much of service to the general practitioner. The arrangement of the chapters according to pathological rather than anatomical classification is to be commended. The symptoms, diagnosis, and treatment are dealt with as fully as possible, considering the limited size of the book. S. J. R.

THE TONSILS AND THE VOICE. By RICHARD B. FAULKNER, M.D. Pp. 381. Pittsburg, Pa.: The Presbyterian Book Store, 1913.

IT is an unpleasant task to be able to say nothing good about a book, but from the first page of this work, where the author's portrait appears as a frontispiece, it is a conglomeration of italics, quotations, and questions in large type with the answers, if there are any, so confused and jumbled up that it makes very tedious reading.

It is attempted to show, apparently, that the function of the tonsil is to aid in voice and tone production and that its complete removal is practically always followed by diastrous results. The book shows evidence of hard work, but as it stands it is thoroughly unscientific and worthy of scant consideration. G. M. C.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Cultivation of the Organism of Epidemic Poliomyelitis.—S. FLEXNER and H. NOGUCHI (*Berlin. klin. Woch.*, 1913, l, 1693) give the details of their successful attempts to cultivate the microörganism of epidemic poliomyelitis. (Only some of the more important facts can be given here.) The method which finally succeeded is one developed by Noguchi in the cultivation of spirochetes. Human ascitic fluid containing a piece of fresh sterile rabbit's kidney was the medium which proved most satisfactory. The exclusion of oxygen is necessary. For this purpose a deep layer of sterile paraffin oil is sufficient. The primary culture seemed to take with greater certainty where an aërobic apparatus was employed. The tubes were kept at body temperature. Flexner and Noguchi found that all tubes that showed turbidity, precipitation, or gas formation within one or two days were contaminated. Even tubes which remain clear or show slight turbidity may be contaminated. To exclude contaminations they removed small quantities of material with sterile pipettes and stained in the usual method, and also made transfers to the ordinary media. Bacteria in the smears or any aërobic growth are contaminations. Having excluded these, Flexner and Noguchi found that the growth of the poliomyelitis organism presented the following characteristics. After about five days in the incubator a faint opalescence is observed in the fluid about the piece of tissue. The controls remained clear or showed a finely granular precipitate about the tissue. In the following three to five days the opalescence in the inoculated tubes spread upward through the fluid while the precipitate in the controls collected more at the bottom of the tube. After ten to twelve days, the diffuse opalescence of the inoculated tubes began to clear

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and a sediment composed of small particles of irregular shape collected at the bottom of the tube. By the use of about 0.2 c.c. of the primary culture, successful transplants can be secured. The material for inoculation was obtained from patients suffering with the disease and from experimentally infected monkeys. Some of the latter material was preserved nine months in glycerin. An emulsion made from this material after passage through a Berkefeld filter gave a positive culture. All the pure cultures obtained from the various sources were examined and showed similar characteristics morphologically and with dyes. In the dark field preparation it is possible with practice to distinguish the organism. It is best stained by Giemsa's or Gram's stain. The organisms are round in pairs, in short chains, or irregular conglomerate masses. The individual organisms reach a size of about 0.2 micron in diameter. The limit of optical definition in a microscopic preparation is between 0.15 and 0.3 micron. It is quite possible that smaller organisms than those observed may exist. In solid media chains are missed. As the culture becomes old, degenerative changes may occur. The organism described above is found so constantly in the central nervous system of diseased men or monkeys that the presumptive evidence of its etiological relationship is strong. In attempting to reproduce poliomyelitis in monkeys cultures which were obtained from human sources as well as from monkeys were used. Inoculations were made directly into the brain or into the nervus ischiadicus and peritoneal cavity. As was to be expected the material obtained from man proved less infectious than that which had already been passed through monkeys. Positive results were obtained with each method of inoculation equally frequent. Cultures which were in their eighteenth or twentieth generation caused the disease to appear in monkeys. Tissues from these infected monkeys were proved to be infective. Furthermore, all the characteristic histological changes of the experimental infection were reproduced in the infected monkeys.

The Production of Acetone Bodies in the Living Animal.—F. FICHLER and H. KOSSOW (*Deut. Arch. f. klin. Med.*, 1913, cxi, 479) conclude from their experimental studies in part as follows: The liver is the organ where acetone and diacetic are formed in the body. It has already been shown that the perfused liver is capable of forming these substances. Furthermore, it is in the liver that B-oxybutyric acid is formed. It is probable that this acid is produced chiefly in the liver, though it is not certain that other organs or tissues are not also concerned in its formation. The fact that an animal whose liver function is partially destroyed produces less of these bodies than one in whom the liver function is normal supports the view expressed above. In so-called reversed Eck's fistula the liver produces excessive amounts of acetone bodies.

The Fatiguability of the Kidneys.—H. MOSENTAL and C. SCHLAYER (*Deut. Arch. f. klin. Med.*, 1913, cxi, 217) have made an experimental study of the fatiguability of the kidney with the following results: The diseased kidney may be exhausted in various ways. The state of renal function determines very largely which diuretic fatigues the kidney and which does not. The kind and frequency of use of the

irritant employed to produce the kidney lesion is also an important factor, as well as the dose of the diuretic. An excess of sodium chloride may increase the fatiguability of a diseased kidney (chromium poisoning), even though it is well excreted. This fatiguability of the kidney is shown experimentally only after giving caffein. In other cases caffein may restore to activity a kidney fatigued by sodium chloride.

The Secretion of Urotropin by the Mucous Membranes.—A. LEIBECKE (*Berlin. klin. Woch.*, 1913, I, 1698) has attempted to determine whether urotropin is secreted in concentration sufficient to inhibit bacterial growth, especially in the middle ear. His results are summarized as follows: (1) Urotropin appears in the urine about one-half hour after it is administered, in the cerebrospinal fluid after three-quarters of an hour, in the milk in one hour, in the ear and bronchial secretions after about two hours and in peritoneal exudates after about four hours. It disappears from the secretion of the ear after fifteen hours, from bronchial pus after thirty hours, from the milk after twenty-one hours, from cerebrospinal fluid after fifty-three to seventy-seven hours. The time intervals are only approximate. (2) The greatest concentration is contained in the cerebrospinal fluid and milk soon after giving the drug. In the exudate from the middle ear, this point is reached only after four to six hours. The same apparently holds true for bronchial pus. (3) In doses of 0.25 to 1 gram the maximum concentrations observed were 1 to 10,000 in the ear, peritoneal pus 1 to 12,000, 1 to 15,000 in cerebrospinal fluid, and 1 to 20,000 in bronchial exudate; the concentration in the milk is the lowest. (4) The concentration of urotropin in cerebrospinal fluid and aural pus in the child in doses of 0.25 and 1.5 grams bears no quantitative relation to the dosage. The body weight of the patient also appears to be of no consequence. (5) No cumulative effect is demonstrable in milk, cerebrospinal fluid or aural pus. (6) It is recommended to give relatively large doses within six or seven hours. (7) In concentration on 1 to 10,000 to 1 to 6000 in aural pus the effect on bacterial growth is doubtful. (8) Injurious effects on kidneys are conceivable with the usual therapeutic dose, but the danger of this is very slight if the patient drinks freely of water.

A Contribution to the Radiological Examination of the Pericardium.—E. v. CZYHLARZ (*Wien. klin. Woch.*, 1913, xxvi, 1394) finds that during deepest inspiration a clear space is seen between the shadow of the diaphragm and that of the heart extending from the apex to the vertebral column in about 75 per cent. of normal individuals. The phenomenon is apparent only for one to two seconds and is lost soon as expiration begins. It is difficult to photograph it satisfactorily, but with practice it can be detected readily with fluoroscopic examination. The phenomenon is due to separation of the two layers of the diaphragm, one of which is attached to the diaphragm, the other to the heart. The presence of the phenomenon, therefore, excludes the possibility of an adhesive pericarditis involving this area. As the phenomenon may not be observed in a certain proportion of normal individuals, its absence is without significance.

The Transmission of Experimental Syphilis to Man.—A. BUSCHKE (*Deut. Med. Woch.*, 1913, xxxix, 1783) considers that Metchnikoff's experiments which tend to show that experimental syphilis is not transmissible to man are inconclusive. He reports a case which came under his own observation which seems to prove the contrary, and believes that it would be very unwise to employ spirochetes from experimental syphilis for vaccination of man, as Metchnikoff has suggested. Buschke was consulted by a man who was employed as assistant in a laboratory in which experimental syphilis was being studied. The patient was thirty years of age, married, and has previously enjoyed good health. He denied venereal infection. April 7, 1913, the patient was assisting at an operation on a syphilitic rabbit. The operator inserted a sterile needle into the syphilitic testicle. As the needle was withdrawn, it was accidentally plunged into the skin of the end phalanx of the patient's left index finger. The patient wore rubber gloves which were immediately removed; blood was squeezed from the small wound, which was then washed with bichloride of mercury and with carbolic acid. Finally the finger was bandaged. The wound healed and nothing more was thought of the accident. About the middle of June the patient began to feel badly. He complained of night sweats, pains in the head, especially above the eyes, and vague general distress, which suggested to the patient influenza. At this time the patient had noticed a small nodule about the size of a pin-head beneath the skin of the last phalanx of the left index finger. By the end of July the general malaise had increased to such a degree that the patient spent his week's vacation in bed. The patient himself now suspected syphilitic infection but did not express his fear and was referred to an oculist because of the constant pain above the eyes. There was now a bluish discoloration about the ulcer on the finger. When Buschke was first consulted August 4, 1913, he found on the left index finger a livid, oval area about 0.5 by 2 to 3 cm. in extent, sharply circumscribed. The skin was slightly elevated, and there was induration. In the left inner cubital region there was a firm, indolent gland about the size of a walnut. Over the abdomen were several erythematous spots. The Wassermann reaction gave complete fixation. In the next few days a maculopapular eruption appeared on the buttocks and extremities. The genital organs and inguinal glands were normal. In the serum obtained from a papule spirochetes were found. The syphilitic infection from which the patient is suffering is quite as virulent as usual, and there can be little doubt that it was contracted in the manner described. The case demonstrates that the disease produced in rabbits by inoculation with human spirochetæ pallidæ is certainly syphilis; that repeated passage through animals does not lessen the virulence of the organisms for man; and that a living vaccine obtained from animals cannot be employed in man.

Hypersensitiveness to Arsenic.—C. STAUBLI (*Deut. med. Woch.*, 1912, xxxviii, 2452) reports two patients treated with sodium cacodylate, in whom acute symptoms developed following injection of the drug. Their hypersusceptibility to the drug resulted in extensive local inflammatory swelling, marked rise in temperature, general malaise, headache, diffuse pains in the joints, loss of appetite, and, in one case, dyspnea.

SURGERY

UNDER THE CHARGE OF

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The Transplantation of the Hair-covered Skin.—PERIMOFF (*Zentralbl. f. Chir.*, 1913, xl, 1443) says that Lauenstein attempted, unsuccessfully, to transplant hair-covered skin from one man to another. He then tried experiments on nine dogs, with indifferent success. On April 6, 1912, Perimoff removed an ugly, star-shaped scar, completely hairless, 10 cm. long and 5 cm. wide, from the temperoparietal region of the scalp, going down to the bone. The patient had requested the operation and had brought with him a man, who, for a consideration, was prepared to sacrifice a portion of his scalp for transplantation to the patient. Healing occurred by first intention and in ten days the patient left the hospital. He returned ten days later when the flap was grown fast. The hair had not fallen out and its growth left nothing to be desired. The patient, an officer, gave his word that he would report again if the hair fell out, but up to the time of the report he had not appeared. Perimoff believes that Lauenstein's failure was due to the fact that the latter used iodobenzine in the disinfection of the skin and that the skin was too much traumatized. Similar experiments on dogs may fail easily because it is difficult to maintain in dogs the unchanged position of the transplanted skin.

The Commandments of Modern Urinary Practice.—CATHELIN, of the Hôpital d. Urologie, Paris (*Amer. Jour. Urology*, 1913, ix, 437) has collected the following principles or commandments, which he offers, particularly, to the general practitioner: (1) Never pass a catheter the first time you see a patient unless compelled. Close clinical examination will almost always enable us to arrive at a diagnosis without it, while its use may lead to very troublesome infection. (2) Never catheterize during an acute attack of gonorrhea. As a rule this procedure is the means of conveying infection to the deeper parts giving rise to prostatitis and spreading to the neck of the bladder and ultimately to the bladder itself. It is in these cases that we must make generous use of purely medical means (diuretics, the balsams and antiseptics). (3) Never syringe the anterior urethra during the acute stages of gonorrhea, for the pus may thus be washed back into the deep urethra which then soon becomes infected in turn. (4) Never dilate when there is too much resistance. A narrowed canal which

yields to gradual dilatation, gives quite contrary results if forced. (5) Never cocainize the canal without urgent reasons. Cathelin has never introduced cocain into the urethral canal. A patient who has pain when catheterized is the victim of bad catheterization. (6) Never omit rectal examination in urinary subjects. This method of examination puts us on the track of the diagnosis and enables us to steer clear of gross mistakes. (7) Always explore with a metal sound when the patient complains of pain in the glands. Spontaneous pain in the glands provoked by passing water is a pathognomonic sign pointing, almost to a certainty, to stone in the bladder. Of course this does not apply to young subjects with gonorrhea, where this pain is customary, for other reasons, but in middle-aged people we must suspect calculus. (8) Always resort to cystoscopy in doubtful cases. There are indeed cases in which no diagnosis is possible otherwise than by actual inspection, such as polypi, ulcers, etc. (9) Always resort to cystoscopy in hematuric patients at a suitable period. In vesical hematuria the suitable period is between the attacks of bleeding; in renal hematurics it is during the actual bleeding in the beginning, because at first the hemorrhages are less profuse and their discovery will enable us to decide which kidney is affected, though this kidney cannot be felt and gives no pain. (10) Always radiograph the upper urinary apparatus in renal cases of uncertain diagnosis. Cathelin regards cystoscopy and the metal sound as sufficient and even preferable for the lower part of the genito-urinary tract. (11) The tuberculous kidney is a small kidney, not palpable and not painful. It may only be manifested by more or less marked cystitis. (12) Evening hematuria is always a calculous hematuria, *i. e.*, hematuria which comes on of an evening is usually bleeding, provoked by the day's work, so that it may fairly be opposed to spontaneous hematuria due to tumor. (13) Never make use of silver salts in urinary tuberculosis. Nitrate of silver while remarkably affective in common affections of the urinary tract, is altogether contra-indicated in tuberculous affections. They get worse when it is used. (14) Tuberculous urine is never ammoniacal. It has no odor.

A Contribution to Malignant Tumors of the Testicle, Especially the Epitheliomatous.—SAKAGUCHI (*Deutsch. Zeits. f. Chir.*, 1913, cxxv. 294) says that the so-called large-celled tumors are the most frequent type of malignant tumors of the testicle (23 out of 32 tumors). The typical large-celled tumors are epithelial and specific for this organ. Because of their situation, the age of the patients, the manner of extension of the tumor cells, and their similarity to the cells of the convoluted tubules, these tumors, in all probability, develop from the epithelium of these canals. Complicated epithelial tumors are found in the testicle, which are made up partly of cuboidal partly of cylindrical tumor cells, and are probably developed from the epithelium of the tubuli recti or canals of the rete testis. This is shown by the site of the tumor, the frequent intracanalicular method of extension of the tumor cells of the rete portion, the cuboidal and cylindrical cells, and the colloidal contents of the same, as well as the similarity of the tumor growth to the exuberances in the regeneration of the rete canals. Sarcoma is found very rarely in the testicle. Only

one occurred in this group of 32 tumors of the testicle. The simultaneous occurrence of cancer and tuberculosis was found only in 1 case. No relationship between the two conditions could be established. It is probable that the tuberculosis was secondary. Glycogen was never absent in the recent large-celled tumors. Even when the preparations were kept a long time in unsuitable fixation fluid, glycogen could be found in a large number of cases. On the other hand, fat could be found only in tumor cells already undergoing degeneration. Elastic fibers in the tumor foci (in sarcoma as well as cancer) were always diminished and finally disappeared. Intracellular infiltration was found in only 5 cases, and then it was not marked. The large-celled epithelial tumors occurred most frequently in the age of greatest strength, the fourth and fifth decade. In 4 cases, the tumor was associated with a history of trauma, in 1 with ectopy. In 13 cases the tumor was on the left side. In 8 the history does not show the side affected.

The Treatment of Dislocation of the Humerus with Fracture of the Head.—CAHEN (*Deutsch. f. Chir.*, 1913, CXXV, 391) says that he has twice, in the past year, made the attempt, after separating completely the fractured head from its ligamentous and other attachments, by placing it in good position on the fractured surface of the lower fragment, to obtain good union. In the first case, a man, aged fifty-two years, this was successful notwithstanding the development of delirium. The functional result, a year after the injury, is so good that the patient has resumed his work in a machine shop. In the second case, a woman, aged sixty-three years, there developed six weeks after complete healing, a fistula in the operation scar. The head of the humerus did not remain fixed in its proper position, and a large fragment was removed a half year later. The active movements of the injured arm at the shoulder are now much limited. In the first case, the *x*-rays show that the upper end of the humerus is still in the dislocated position. The patient can raise the operated arm forward to 20 degrees above the horizontal. Passively, the arm can be raised completely.

Operation on Perforated Stomach and Duodenal Ulcers.—SEIDEL (*Zentralbl. f. Chir.*, 1913, xl, 1481) says that the two chief indications in the early operative treatment of these perforated ulcers, are: To close the perforation, and to reëstablish the conditions which will prevent postoperative obstruction to the escape of the stomach contents into the intestine. The most reliable method of closing the perforation is always by suture. Seidel has never found it necessary to deviate from this principle, and succeeded in thus closing the perforation, without great difficulty, in 19 cases. It is not necessary that specially favorable conditions must be present. He found in some of his cases callous changes, very large ulcers, as well as saddle-shaped ulcers of the lesser curvature with perforation on the posterior wall. He says that the closure of the perforation depends alone on the technique. The sutures must be placed as far as possible from the edges of the perforation. In very small ulcers the sutures should encompass all the callous tissue. In very large ulcers it should grasp

the greatest part of this tissue and turn it in. The first row of sutures are made with thick silk and pass through the whole wall of the stomach into its lumen. A row of sutures reaching to the non-infiltrated tissues, or a flap from the greater or lesser omentum, reinforces the through-and-through sutures. In his last 7 cases he employed the following method of preventing cutting of the sutures: On two sides of the circumference of the perforation, 1 cm. or more from the edges of the perforation, are passed one or two supporting sutures, somewhat parallel to the margins of the perforation and reaching to the lumen of the stomach. They are not tied tightly enough to fold or cut through the friable tissue. The real closing sutures, also of silk, are then passed from one side to the other, *i. e.*, at right angles to the supporting sutures, reaching outside of the latter and passing through the stomach wall into its lumen. If these are not tied too tightly the perforation is closed without danger of the sutures cutting through. A row of Lembert sutures or an omental flap will complete the watertight closure of the perforation. In 14 of his 19 cases, in which he employed the sutures without further aid in closing the perforation, there have been up to the present time, no disturbances in the passage of the stomach contents, not even in cases in which there had been a marked stenosis at the pylorus.

Alcohol for the Prevention of Acute Cocaine Poisoning.—HERZFELD (*Zentralbl. f. Chir.*, 1913, xl, 1705) says that he has obtained repeatedly from minimal doses of cocaine (Scleich's infiltration narcosis), mild symptoms of poisoning. Dentists have had a large number of deaths from this cause. From inquiry of a number of surgeons he found that some regarded morphin as the antidote *par excellence*, and that an injection of morphin was completely sufficient in these cases. Herzfeld says that morphin has caused many deaths in many cases of cocaine and atropine poisoning. He gives every patient, without exception, 25 to 50 c.c. of whisky or cognac, by the mouth, before the first injection of cocaine. In long-continued operations he repeats the dose, mixing the whisky with sugar water in women and children. In the course of the last four years, he has not had the slightest trouble from local anesthesia with cocaine.

Interparietomuscular Pyloropexy as a Method of Closing the Pylorus in Gastroptosis with Gastrectasia.—MARIANA (*Zentralbl. f. Chir.*, 1913, xl, 1706) says that he operated on 2 cases with death from ether pneumonia in the first, and in the second healing with the best functional results. After performing a posterior gastro-enterostomy near the pylorus, he fixes the sharply bent pylorus by suturing it to the margins of the right rectus muscle in the wound, a little below the costal arch. The fixation of the sharply flexed pylorus in the abdominal wound, closed the pylorus, served as a suspension, and thus improved the function of the gastro-enterostomy In his second case, it was shown by the *x*-rays that the greater curvature of the stomach, before the operation, reached almost to the pubis, while after the operation it extended to about the umbilicus and occupied a transverse position. The *x*-rays showed also that the bismuth food no longer passed through the pylorus but through the anastomotic opening.

THERAPEUTICS

UNDER THE CHARGE OF

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Clinical and Laboratory Salvarsan Relapses and their Remedy.—HEIDINGSFELD (*Jour. Amer. Med. Assoc.*, 1913, lxi, 1598) is firmly of the opinion that no case of syphilis can be satisfactorily treated unless the treatment is controlled by the Wassermann reaction. In 651 cases, 3304 Wassermann examinations were made, and salvarsan was administered 952 times. The administrations were made in ambulatory private practice and not a single administration was attended by any incident of untoward character. The initial dose was almost uniformly 0.6 gm. of salvarsan and 0.9 or 0.6 gm. of neosalvarsan; if neosalvarsan was repeated within from thirty to sixty days, 0.3 gm. was usually administered, unless persistent lesions or an unchanged or strongly positive Wassermann indicated otherwise. A Wassermann examination was made prior to the initial administration and was repeated every thirty days, until the blood became negative. When the fixation test remained negative two successive times, the examination was repeated in sixty days, if then negative, in ninety days, and then at intervals of six, nine and twelve months, according to the special indications of the case. Deducting 209 cases which were observed less than ninety days, or could not be intelligently followed for the reason of only one Wassermann examination, in 339 out of a total of 442 cases, or 77 per cent., the patients proceeded to recovery from a combined clinical and laboratory point of view, as a result of one or more administrations of salvarsan. No other adjuvant was employed, although 276 cases of somewhat long standing received some form of antisyphilitic treatment prior to the administration of salvarsan. Of the 103 cases, or 23 per cent., of salvarsan failures, nine received no additional attention. Of the remaining 94 cases, 13 proceeded to clinical and laboratory recovery with the aid of mercurials and 23 with the aid of atoxyl and sodium cacodylate: 21 have been observed comparatively too short a time to pass definite judgment; 22 cases have apparently failed, from at least a laboratory point of view, with all methods of treatment. Summarized, in 50 per cent. of salvarsan failures the cases have proceeded to complete clinical and laboratory recovery when the treatment was supplemented by other measures. In 371 cases, for the most part old and long-standing infections, some form of previous mercurial treatment has been received. Of these, 230 cases proceeded to recovery and 95 could not be intelligently followed. In other words, 83.5 per cent. proceeded to absolute recovery from a clinical and laboratory point of view. This is of striking interest, as it shows that more cases (83 per cent.) proceeded to salvarsan recovery when previously treated with mercury, than those cases (61 per cent.) which had received no previous mercurial

treatment. This past apparently indicates that previous mercurial treatment favorably influences syphilis for salvarsan treatment. It may be, however, that the percentage of recovery is higher in the cases previously treated with mercury for other reasons: A large percentage of these cases were of rather long standing, with weak positive, negative or almost negative Wassermann. Some possessed a dubious history, enveloped in greater obscurity by a too early administered mercurial treatment. The cases not previously treated with mercurials were, almost without exception, comparatively recent infections, personally observed, in which present-day methods of greater accuracy substantiated the diagnosis. It is evident from this that salvarsan failed to effect a satisfactory result from a clinical and a complement-fixation point of view, in 23 per cent. of the cases treated, and salvarsan aided by other measures in about 12 per cent. Some of the "failures" were in cases which were rapidly advancing in spite of treatment. The majority of the "failures" however showed no clinical manifestations but gave a persistently strong positive Wassermann. Heidingsfeld believes that salvarsan, though not an unfailing remedy, is by far the most effective agent which we possess for the treatment of syphilis. It affects an apparent clinical and laboratory cure in about 77 per cent. of the cases treated. A large proportion of the remaining 23 per cent. of cases with the aid of other measures, gives every promise of proceeding to a negative Wassermann and absolute clinical cure in due course of time.

The Dose and Methods of Application of Radio-actve Substances in Internal Medicine.—GUDZENT (*Berlin klin. Woch.*, 1913, l, 1597) has experimented in order to secure a more uniform dosage of radium emanations as given by inhalation. He believes that doses of from three to five Maché units per liter are as efficient therapeutically as the higher concentrations. He also says that nervous and anemic patients do not seem to bear the larger doses as well, and since they are no more effective therapeutically, he advises against their use. He believes that the most efficient method of giving the radium is by inhalation. Gout and chronic articular rheumatism are most influenced by radium treatment and especially when the radium is given by inhalation. Sciatica, diabetic neuralgias, and Basedow's disease are also very much improved by this method of treatment. With reference to the use of other radio-active substances such as thorium and tharium X. Gudzent is of the opinion that the results obtained with their use have been decidedly inferior to those obtained with radium.

Therapeutic Pneumothorax as a Palliative Measure.—DUNHAM and ROCKHILL (*Jour. Amer. Med. Assoc.*, 1913, lxi, 826) report 20 cases of pulmonary tuberculosis treated by artificial pneumothorax. The article emphasizes the value of this treatment as a palliative measure and the value, almost the necessity, of safeguarding the treatment by the use of the Röntgen rays. In emphasizing therapeutic pneumothorax as a palliative measure they do not deny its value as a curative one, but they do not feel that they have had sufficient time, experience or results to attribute to it this superlative value. They

say that the results and effects of this therapy are positive. The principal pathological findings after collapsing the lung are that the cavities are emptied, in part or in whole, according to the extent of the pleural adhesions, caseous areas have become cicatrized, and above all, an extensive overgrowth of the fibrous tissue is permitted during the enforced rest of the lung. The clinical effects of the induced pneumothorax are shown by a fall in temperature and a reduced number of night sweats, increased strength and appetite and finally gain in weight. These effects are all due to lessened absorption of toxins. The cough and sputum are greatly lessened and the number of tubercle bacilli in the sputum diminish. This treatment is of especial value in the control of pulmonary hemorrhages. Cases for this method of treatment should be carefully selected, but the indications for the proper selection of suitable cases is, as yet, not entirely clear. They consider frequent Röntgen-ray examinations most important in order to determine the proper time for refilling. The amount of nitrogen injected should be just sufficient to keep the lung collapsed and no more. Dunham and Rockhill conclude that this treatment is palliative and offers relief when usual methods of treatment have been unsuccessful. While it will possibly never become a routine treatment for tuberculosis, its use will certainly be indicated for those with quiescent lesions of one side and acute recrudescence of the other, and for such advanced cases as may at least profit by the certain amelioration of clinical symptoms. By the use of stereoscopic röntgenograms it is possible to select cases suitable for the treatment, to watch the progress of the disease, to determine the extent of the lung collapse, to note the pressure on the heart and mediastinum, to exclude pleural effusion and especially to watch the progress of the disease in the uncollapsed side.

The Röntgen Ray Treatment of Ring-worm.—Emrys-Jones (*Brit. Med. Jour.*, 1913, pp. 849, 2753) basing his conclusions upon 200 cases of ring-worm treated by Röntgen rays, considers that this is the best and much the greatest method of treating this disease, particularly when the disease is extensive and well-established. He uses the single dose method, that is one exposure is given to any portion of the infected area. At times a single exposure is incomplete and this necessitates further treatment. He has never had a burn, although 93 of the cases were infected over the entire scalp. The technic and details of this method are given in the article. Emrys-Jones says that, with proper apparatus and in expert hands, this method is perfectly safe.

Pneumothorax Treatment of Tuberculosis of Lungs.—Amrein and Lichtenhahn (*Quart. Jour. Med.*, 1913, vi, 487) report 11 cases of pulmonary tuberculosis in which they produced an artificial pneumothorax by injecting nitrogen for purpose of treatment. The cases are reported in detail. In six of the eleven distinct and marked benefit was obtained. The chief results of the treatment were the disappearance of fever and other toxic symptoms, the diminution of cough and expectoration and the checking of hemoptysis when it was present. The remaining five cases were not so definitely successful. Amrein and Lichtenhahn believe that by this method of treatment many

apparently hopeless cases of pulmonary tuberculosis can be arrested, and, further, may be healed and even if satisfactory results are few and far between, the trial of the treatment is legitimate. The article also includes a short résumé of the literature upon the subject of induced pneumothorax and Amrein and Lichtenhahn discuss briefly the different methods of producing it. They prefer the Murphy–Brauer method by a preliminary incision down to the parietal pleura. The induction of an artificial pneumothorax must always be controlled by a suitable manometer. The amount of gas introduced into an individual case is dependant upon the presence or absence of pleural adhesions and they have injected as much as 1000 c.c. of nitrogen. It is also important to have an *x*-ray examination before an attempt is made to produce a pneumothorax principally to determine whether the other lung is sound or not. Moreover the *x*-rays are of great value in comparing conditions at subsequent refillings of the pleural cavity.

Eucalyptus Oil in Scarlet Fever and Measles.—ELGART (*Med. Klin.*, 1913, ix, 1251) acting upon Milne's suggestion has used eucalyptus oil for the prevention of scarlet fever and measles. Milne advised inunction of the entire body with the oil but Elgart has had equally good results by the use of a bag soaked with the oil which is worn around the neck by those exposed to contagion. In this way the children inhale the fumes constantly and the room is kept saturated with the fumes. Milne during the past thirty years has had 245 cases of scarlet fever and 234 cases of measles in a total of over 12,000 admissions to boys' homes of which he is in charge. The cases were all imported and no epidemic resulted even without isolation of the sick children.. This result was attained, according to Milne, by merely rubbing the patients from head to foot with the eucalyptus oil twice a day for the first four days and then once a day for six days. In addition the tonsils were swabbed with 10 per cent. phenol in oil, at first every two hours and then at longer intervals. Elgart advises the use of the eucalyptus oil for everyone exposed to the infection in addition to its use by the patients themselves. He also prefers the inhalation of a 30 to 50 per cent. solution of lime as a means to free the throat from the infecting bacteria and advises these inhalations as a prophylactic measure. In brief Elgart would not only render the patients themselves less contagious but would render those exposed to contagion less apt to contract the disease. With respect to the treatment of scarlet fever—Elgart says that few of his scarlet fever patients, on systematic inhalations of lime, developed complications and those complications which developed were mild and short in duration. He believes that his method is efficacious in preventing the spread of infection, in shortening and attenuating the course of both scarlet fever and measles. Milne's method is, according to Elgart, especially adapted for the prevention of scarlet fever and measles in various institutions.

"Specific" Use of Salicylates in Acute Rheumatism.—MILLER (*Quart. Jour. Med.*, 913, vi, 519) in an endeavor to answer certain objections that have arisen with regard to the action of the salicylates in acute rheumatism, says that the objection that the larger doses

of salicylate do not imply increased absorption of the drug is without foundation. The objection that the larger doses are too prone to produce vomiting to be of value is only partially true. The production of vomiting is more a matter of the type of case under treatment and the methods of administration than the size of the dose employed. The vomiting produced in severe cardiac cases must necessarily be a limitation to any anti-rheumatic action which the drug may possess in rheumatic carditis. The objection that large doses are too prone to produce acid intoxication to be of value is also only partially true. The method of administration is of more importance than the size of the dose. The objection that the larger doses are dangerous and tend to increase fatalities, is not supported by the series of cases Miller examined. It is again a question of knowing how and when to use the drug. The objection that the specific use of salicylate is unsound, as relapses, particularly of nodules, are not prevented, is not well supported by the series of cases examined. Most of the relapses occurred on or after small doses or a short period of administration of the drug; cases taking large doses showing some immunity to relapses. Nodules are not generally more commonly found in relapses than are other manifestations, and where they develop under large doses it seems that they signify little, if any, fresh activity on the part of the infection.

PEDIATRICS

UNDER THE CHARGE OF

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The Meningeal Form of Poliomyelitis.—ARNOLD NETTER (*Brit. Jour. Child. Dis.*, 1913, x, 531) discusses the meningeal forms found in the epidemic of poliomyelitis existing in France for the last four years. Wickman defined the "meningeal form" as those cases simulating cerebrospinal meningitis, simple meningitis, or even tuberculous meningitis, with the symptoms of violent onset, high temperature, vomiting, headache, pains in the back and limbs, rigidity of trunk and neck, and Kernig's sign. Paralysis usually appeared after several days and might be transitory and ill-marked, but was more frequently persistent and followed by muscular atrophy and deformity. In some cases the clinical picture remained that of meningitis exclusively, whether recovery or death took place. The pathological anatomy of cases fatal at an early stage has always shown the pia mater infiltrated with cells, and lumbar puncture shortly after the onset shows an albuminous and fibrinous fluid rich in cellular elements. An erroneous diagnosis of cerebrospinal meningitis has been made in a number of cases. The cerebrospinal fluid gives valuable information. In a fair number of cases of meningococcal meningitis the fluid is almost trans-

parent during the first thirty-six hours, and contains only a few cells. On the other hand, the fluid in the early stages of these cases of poliomyelitis is definitely fibrinous and rich in cells, many of which may be polymorphonuclears. Great importance is attached to the knee jerks which are often lost at an early stage, and to the presence of pain in the limbs which appears more marked than in other forms of poliomyelitis. The seasonal incidence is of value, poliomyelitis being more frequent in summer and autumn and meningitis in the spring. The co-existence of typical cases is also a help. Poliomyelitis with meningeal onset has been especially frequent in France. In one study of 58 cases it was found in 29 per cent. In other studies throughout France the percentage has been at least as high. Several epidemics erroneously termed cerebrospinal meningitis have subsequently shown their true character by the development of muscular paralysis and atrophy.

Whooping Cough in the First Days of Life.—E. A. COCKAYNE (*Brit. Jour. Child. Dis.*, 1913, x, 534) furnishes interesting testimony of older writers on congenital whooping cough. He cites a number of writers, such as Sir Thomas Watson, Rillet, and Barthey, who mention infants who had characteristic fits of coughing on the first day of their lives, the mother having had whooping cough during the last months of pregnancy. The case described by Cooper Cole was probably congenital. The mother developed pertussis in the sixth month of pregnancy. The child, born at the eighth month, began to cough on the third day, and whooped on the seventeenth day, the attack being typical and severe. If this case were congenital it would show that the organism may be found in the circulating blood or remain virulent in the placental tissues for nearly two months after onset of disease. Pertussis in the newly born acquired after birth is more numerous, but even this is seldom met with. Bouchut reports a case in which an infant aged four days, two days after exposure to infection, began to cough and whooped eight days after birth. Numerous cases are mentioned where infants developed pertussis when ten, twelve, and fifteen days old. Cockayne reports a case of his own in which the infant began to cough at the age of five days. The incubation period must have been four days or less, its mother and a brother developing the disease a few days before its birth. The disease in the infant was typical and the blood examination showed a characteristic leukocytosis with increase of the lymphocytes. The disease in young babies is often atypical, there being no "whoop," but a more paroxysmal character in the coughing than is usual in mere bronchitis.

"Tic" in Children.—PHILIP F. BARBOUR (*Pediatrics*, 1913, xxv, 697) illustrates several cases of "tic" and shows the difference between this condition and chorea. In the case of a girl said to have chorea, the prominent symptom was a quick movement of the head from side to side every few minutes. The fact that the child had rheumatism might further complicate the diagnosis. The following tests, however, indicate the differentiation. When her tongue is protruded it is held perfectly still and she has perfect control of its

movements. In chorea it would be protruded in an uncertain and irregular manner, and would probably be drawn into the mouth quickly without apparent control. In her hand-grip there is no irregularity or failure in coördination in reaching for the hand, as would be the case in chorea, and the contraction is firm and persistent. When asked to do voluntarily the movements of the head which she appears to be doing involuntarily, she moves her head from side to side with perfect rhythm and regularity. There is no exaggerated jerking of the head as in chorea. In another case referred to the face was grimaced. Barbour mentions here the relationship between local irritation and this form of tic. Cures have frequently followed operations which relieved the irritation and whether it is true or not that the basic factor is a neuropathic substratum, one should persist in removing local causes of disturbance. In chorea there is inability to coördinate the muscles for a specific purpose. In tic there is coördination to procure certain results, but coördination is repeated until it becomes impulsive rather than volitional. The inability to resist the desire to make certain coördinated movements assumes a type of obsession, a basic factor differing markedly from chorea, and placing the disorder within the realm of psychical defects. The original purpose for establishing a habit of coördinating certain muscles is hard to determine, but may be the itching of an eyelid, or the wearing of a tight collar which induces a shrugging movement. Patrick, of Chicago, suggests the most rational treatment in these cases. It consists in making the movements volitional, so that instead of remaining as an unconscious habit, the patient will think about the movement he makes. No treatment offers very optimistic results in these cases, but the method mentioned seems to offer the most favorable outcome.

Pyuria in Infancy.—THEODORE J. ETTERICH (*Pediatrics*, 1913, xxv, 702) makes a plea for the more careful and routine examination of the urine in young children because of the frequency of acute pyelitis and the fact that many of these cases are mistaken for typhoid fever, malaria, and dentition fever. His remarks are based on 19 cases of acute pyelitis under his observation. All were females and ranged in age from seven months to eight years. The condition may be primary, but is often secondary to gastro-intestinal disorders, influenza, and other infectious diseases. The colon bacillus was found in 4 of his cases. In very young children this condition is remarkable for its lack of distinctive features. Fever is usually high and of the remittent type, and continues in the acute cases from three to six weeks. No chills, convulsions, or nervous symptoms occurred in any case, and there was nothing to explain the fever until the urine was examined and pus was found. The urine is very acid in reaction, the specific gravity usually low, and numerous pus cells and albuminous debris is found. The general health was, as a rule, not markedly impaired. Pus was often present in the urine several weeks after the patient had fully recovered. There were no relapses and no deaths. The treatment was potassium citrate gr. v every three hours until the fever subsided. Then urotropin in 1-grain doses four times a day.

OBSTETRICS

UNDER THE CHARGE OF

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The Treatment of Puerperal Sepsis at the Sloane Hospital for Women.—WILBUR WARD (*Amer. Jour. Obstet.*, March, 1913) states that in the last 8000 cases at the Sloane Hospital the septic mortality was 0.0485 per cent. A marked decrease in mortality and morbidity followed the routine use of rubber gloves. Another striking point is the fact that in cases treated by Cesarean section previous examination and manipulation greatly increased mortality and morbidity. Section should be declined in cases that have been much interfered with before they are brought to hospital. In prophylaxis, surgical asepsis is strictly used, and all interference, whether by examination or douching or the use of instruments, is limited as far as possible. In the presence of sepsis uterine drainage should first be secured by vaginal or intra-uterine douches with salt solution. If no improvement follows the uterus should at once be explored, and only once with the gloved finger, and then in the gentlest manner possible. Should secondary foci arise they are to be treated in accordance with the circumstances of each case. Especial stress is laid upon the general supporting treatment.

Rupture of the Uterus.—An interesting case of rupture of the uterus in early pregnancy is reported by NOON, in St. Bartholomew's Hospital (*Jour. Obstet. and Gynec. of the British Empire*, October, 1912). The patient was supposed to be pregnant about three months. Hemorrhage was followed by pain and by the expulsion of the fetus. A physician who was summoned gave the patient chloroform, and said that he had removed the after-birth. On the following day she was admitted to hospital with normal pulse and temperature. The fundus of the uterus could be palpated just above the symphysis, the cervix admitted one finger, and there was no bleeding. Three days afterward, while straining, the patient felt as if a lump were coming down into the vagina, but she had no pain. On the following day, while straining after an enema, a red matted swelling appeared at the vulva. She was at once removed to the operating room and anesthetized. Upon examination, a protruding mass consisting of coils of small intestine matted together and covered with lymph was found. These were separated and the lymph peeled off. The tissues were thoroughly irrigated with salt solution. The intestine had come through the cervix, which was closing down upon them, and as the uterus seemed healthy they were replaced through the cervix and the uterine wall into the abdomen. A large tear was then felt across the fundus of the uterus. The patient was placed in the Fowler position, and the uterus, Douglas's pouch, and the vagina irrigated with salt

solution. The uterus and vagina were packed with sterile gauze, a large pad was placed over the vulva, and a T-shaped bandage applied. She apparently recovered without incident. Seven months afterward she returned, stating that she had suffered from abdominal pains like colic, chiefly in the right iliac fossa. Vomiting had developed with constipation, diarrhea, and emaciation. Upon examination, she was pale, anemic, thin, with subnormal temperature, and fairly good pulse. The abdomen was full but not distended, there was no rigidity, but slight tenderness in both iliac fossæ. The vagina, uterus, and rectum were normal, and enema returned clear. The patient passed flatus through the bowel, but vomited. At operation, extensive adhesions were present, and a piece of the iliac colon was found firmly adherent to the parietal peritoneum in the right lower abdomen. This was freed, and the raw surface on the bowel covered by peritoneum. Coils of small intestine were found adherent to the fundus, and, on separating this mass, the bowel was opened in two places. Upon examination, a proximal piece of the bowel was patent, but the lumen of the distal piece admitted only the tip of a pair of forceps. This constriction was divided, and end-to-end anastomosis made. Another loop of intestine was adherent to the bladder and was separated and repaired. The lower part of the wound was drained by a rubber tube. The patient made a good recovery.

Repeated rupture of the uterus within eleven months is reported by HEIL (*Monatsschr. f. Geburts. u. Gynäk.*, 1912, Band xxxv, Heft 3). The second accident was followed by death from septic infection. In each case the rupture was spontaneous.

A similar case is also reported by GOLDSCHMIDT (*Monatsschr. f. Geburts. u. Gynäk.*, 1912, Band xxxv, Heft 3) in a patient in her second pregnancy, who after her first labor suffered from septic infection. At the end of the second pregnancy she suddenly collapsed without having had genuine labor pains. She had, however, suffered from abdominal pain and from very strong fetal movements. The physician who first saw her diagnosticated separation of the placenta, and the patient was brought in a motor car to hospital. There rupture of the uterus was diagnosticated. On section a full term child was found in the abdomen, with free abdominal hemorrhage. The uterus had ruptured at the fundus and the placenta was adherent. Extirpation of the uterus and tubes was performed, the ovaries remaining. The recovery of the patient was uncomplicated.

BROADHEAD (*Amer. Jour. Obstet.*, April, 1912) reports the case of a patient, aged thirty-three years, a multipara, in whom the abdomen was pendulous, tense, and difficult to palpate. Labor pains persisted irregularly for five days, about three weeks before the expected termination of pregnancy. The membranes ruptured spontaneously. When the patient was seen, she was having no pains, and the cervix was not dilated. The head was not engaged, and it was stated that an unusual quantity of amniotic fluid had escaped. The patient was not seen again for several days, when dilatation was advanced sufficiently to admit one finger. The head was not engaged. Her physician supposed that she was in beginning labor, and left the patient, instructing her to send when pains developed. When next summoned, he found her in acute shock with the history of having

one severe pain, followed by complete cessation. The patient's night-dress was saturated with fresh blood, her abdomen was flaccid, and the fetus was easily made out in transverse position, the head to the right and near the umbilicus. There was no presenting part at the superior strait. Upon vaginal examination, the cervix admitted one finger only, and two old scars were present in the cervix. The patient died before she could be transferred to hospital, and no autopsy could be obtained.

Repeated spontaneous rupture of the uterus is described by BECKER (*Zeitschr. f. Geburts. u. Gynäk.*, 1912, Band lxxi, Heft 1 and 2). He has collected 27 cases of repeated spontaneous rupture from the literature of the subject, to which he adds his own. The patient was a primipara, aged twenty-two years, who had hemorrhage at the end of pregnancy, without dilatation of the cervix. When a physician was summoned, he found the membranes ruptured, the os two-thirds dilated, and the head firmly wedged in the pelvic cavity, and no uterine contraction. Two days later a consultant saw the patient, when septic infection had developed. Craniotomy was then done, and as the fetal body was removed bubbles of foul gas escaped from the uterus. On examining the uterus with the hand, a complete rupture transversely across the posterior wall was discovered, and the placenta had separated and was readily removed. The uterus contracted well and there was no hemorrhage. In view of her critical condition and her surroundings, she was treated by drainage with iodoform gauze. Although severely ill she gradually recovered. Six years later another pregnancy occured, when the patient went to seven months, when fetal movements ceased, accompanied by hemorrhage. The cervix was closed; there was some irregular pain, which gradually ceased. The pulse was strong, and gas escaped from the intestine. The patient refused to enter the hospital. Symptoms of peritonitis with septic infection developed, and the patient was finally brought to hospital. Upon examination, diffuse peritonitis was present, and an effort was made to empty the uterus by combined version. This was accomplished without great difficulty, and a macerated fetus and placenta were removed. Upon examination a tear upon the left side of the uterus was found, through which the hands passed into a cavity at the site of the contracted uterine body, and in this cavity were coils of intestine. Section was performed, but the death of the patient followed. Upon examination, no evidence was present of the first rupture, as the uterus had been completely restored. The laceration had occurred at the site of the old rupture, and upon microscopic examination it was found that the muscular tissue of of the uterus at that point had been replaced by connective tissue.

GYNECOLOGY

UNDER THE CHARGE OF

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Tuberculosis of the Cervix.—In view of the extreme rarity of this condition, it is quite remarkable that BENDER (*Rev. de Gyn. et de Chir. Abdom.*, 1914, xxii, 29) should have had the opportunity of observing 2 cases within a short space of time. In the first case he did not suspect the true nature of the condition at the time of operation, which consisted merely in amputation of the cervix for a supposed mild-grade cervical metritis; histological examination of the tissue showed, however, the presence of typical tuberculous changes. A short time after this, Bender had occasion to operate upon a woman, aged thirty-four years, who applied for treatment on account of a mucopurulent leucorrheal discharge, associated with dull pains in the lumbar region. She had had three healthy children, and one miscarriage, the latter about nine months before coming under observation. On examination, the cervix appeared large and indurated; the surface was granular, and somewhat friable, bleeding easily upon palpation. The appearance was not characteristic of cancer, and yet it was obviously not a simple cervicitis, so that a suspicion of tuberculosis was aroused in Bender's mind—a suspicion which was confirmed by histological examination of a small bit of tissue excised under local anesthesia. The patient's general condition was excellent, nothing suggestive of tuberculosis elsewhere in the body being discoverable. In view of the excellent results which had followed the simple trachelectomy in the former case, Bender deliberately chose the same conservative procedure in this instance, first, however, dilating the cervix and making a thorough digital exploration of the interior of the uterus, to assure himself that there were no gross evidences of its involvement. The cavity was then curetted, and swabbed out with iodine, the cervix being then amputated in the ordinary manner. Histological examination of the tissue showed typical tubercles, with caseation, and giant-cell formation; in slides stained for tubercle bacilli, these were found in considerable numbers. Notwithstanding that over two years have now passed since these operations, both patients are well, and show not the least sign of recurrence. Bender thinks, therefore, that in these, evidently early cases, with no sign of involvement beyond the limits of the cervix proper, he was justified in doing the conservative operation, though he does not wish to be understood as meaning to imply that this will suffice for all cases of tuberculosis of the uterine cervix.

The Role of Tuberculosis in the Production of Cystic Neoplasms.—In conjunction with the article, reviewed last month, by Pollosson and Violet upon tuberculosis as an unsuspected factor in the produc-

tion of ovarian cysts, a discussion of the same general subject by PONCET and LERICHE (*Lyon Chirurgical*, 1914, xi, 1) is of considerable interest. These authors state that in 1906 they propounded the theory that many apparent *tumors* are, in fact, nothing but neoplastic structures, which have developed as the result of some mechanical, toxic, or infectious irritant, expressing at the same time the belief that among the latter group, tuberculosis plays an important role. They now state that they have become even more firmly convinced that tuberculosis is the great cause of benign cystic neoplasms in various parts of the body. They have already demonstrated this with regard to cystic adenomas of the thyroid, and now wish to call attention to the frequency with which cystic ovarian tumors, not specifically tuberculous, are found in conjunction with tuberculous tubes. They report an example of this condition occuring in a woman, aged thirty years, in whom a large cystic ovary, and a microcystic oöphoritis were found in conjunction with a frank tubal tuberculosis, a state of affairs exactly analogous to some of those published by Pollosson and Violet. Poncet and Leriche ask, "Is it not rational to conclude, that in the presence of the same infection the tissues may react differently, the ovary being inherently very refractive to a frank tuberculous invasion, but very prone to neoplastic changes?" They do not mean to imply for a moment, however, that all simple ovarian cysts are of tuberculous origin, but merely to call attention to the fact that this is one cause that is often unrecognized.

Cysts of the Cervix Uteri.—There are two kinds of cystic structures which may occur in the region of the cervix, cystic tumors (*i. e.*, cystic degeneration of fibromata, sarcomata, etc.), and *true cysts*, which develop independently of any other uterine affection. Although the latter are exceedingly rare, DAMBRIN (*Arch. mens. d'Obst. et de Gyn.*, 1914, iii, 41) is able to report 2 cases that have recently come under his observation. The first case occurred in a multipara, aged forty-five years, who applied for relief from a mass which she herself noticed in the vagina, and which appeared at the vulvar orifice. On examination, an elliptical, smooth, bluish-gray, somewhat elastic feeling tumor, about the size of a hen's egg, was found attached to the posterior lip of the cervix by a pedicle as thick as the little finger. It was removed under local anesthesia, by cutting completely around the base of the pedicle. On opening the cyst, a second, smaller one was found within. Microscopic examination showed the walls to be composed of fibrous tissue, with a few scattered muscle fibres; it was covered externally by stratified squamous epithelium, the cyst cavity, however, being lined by a single layer of columnar cells. Throughout the fibromuscular wall were numerous glands of the cervical type, surrounded by areas of inflammation; some of these glands showed a distinct tendency to cystic dilatation. The second case occurred in a patient, aged thirty-two years, who had suffered with a prolapse of the uterus ever since the birth of her only child, six years previously. This patient also noticed herself a smooth tumor mass in the vagina. Examination revealed the presence of a rounded, conical-shaped tumor, the size of one's fist, projecting from the vulva. It was covered by vaginal mucosa, which appeared normal, except that the rugæ had

been smoothed out from stretching. Posteriorly, the cyst was attached to the anterior lip of the cervix, but anteriorly it was so intimately associated with the anterior vaginal wall that its exact delimitation was impossible. At operation, no plane of cleavage could be found here, and it was necessary to resort to sharp dissection with scissors in order to free the cyst, during which process it was ruptured, with the discharge of a quantity of blackish, tar-like material. A portion of the cervical lip was excised with the posterior portion of the cyst wall. The walls of the cyst were about 2 mm. thick, and were covered on the external surface by vaginal mucosa; the lining of the cyst cavity in this instance, however, was composed likewise of stratified squamous epithelium, no cells of the columnar type being found anywhere. Dambrin considers that all true cysts of the cervix may be divided into two groups: (1) Mucous cysts, of inflammatory origin, arising from the normal cervical glands as a result of obliteration of their outlet, and being, therefore, entirely analogous to the small, exceedingly common "ovula Nabothii." (2) Cysts arising from epithelial remains of embryonal structures in the uterine wall. Both remains of the Wolffian system (Gärtner's duct), and of the Müllerian ducts come into consideration here, the former much more frequently than the latter, however. In the case of cysts lined by *squamous* epithelium, such as the second specimen described by Dambrin, he considers the origin from Müllerian remains beyond question, but where the cyst is lined by *cylindrical* epithelium, as in his first case, the problem becomes more difficult. If the cells are definitely ciliated, or if a fairly definite muscle layer surrounds the cyst cavity, an embryonic (Wolffian) nature may be assumed, but where these characteristics are absent, the diagnosis from a mucous cyst, of inflammatory nature, may be exceedingly difficult or impossible. Such is the situation with regard to the first case reported, though Dambrin is inclined to place it in the inflammatory rather than in the embryonal group.

HYGIENE AND PUBLIC HEALTH

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Experimental Beriberi.—Wellman and Bass (*Amer. Jour. Tropical Diseases and Preventative Medicine*, August, 1913, i, No. 2, p. 129). report a series of experiments to determine what common articles of diet other than rice will cause polyneuritis in fowls, and especially to ascertain whether the glucose and talc found on commercial polished rice, as milled in local mills, is the cause of polyneuritis. They found that in chickens fed exclusively on polished rice, *ad libatum*, the average daily consumption of glucose was 0.125 grams per day and of talc

0.0625 grams per day. It was found that when glucose was fed in amounts fifty times as much as a fowl would get in an exclusive diet of polished rice, and talc in amounts one hundred times as much, that neither will produce polyneuritis in fowls. It was then found that the glucose and talc, added in large amounts to rice polish, in no way prevents the cure of polyneuritis. The various foodstuffs used by Wellman and Bass in their experiments and the number of days it took to produce a polyneuritis follows: Sago, 20½ days; boiled white potato, 24½ days; boiled milled rice, 27 days; corn starch, 32 days; milled rice, 33 days; wheat flour, 34 days; corn grits, 36½ days; boiled sweet potato, 38 days; cream of wheat, 39 days; puffed rice, 39½ days; macaroni, 40½ days. As a result of their work Wellman and Bass conclude as follows: (1) Glucose and talc, when fed together or separately do not produce *polyneuritis gallinarum* in birds receiving a diet which does not itself produce the disease. (2) Glucose and talc in large amounts do not prevent prompt recovery from *polyneurotis gallinarum*. (3) *Polyneuritis gallinarum* can be produced by feeding milled rice and many other food substances which have neither glucose or talc on them. (4) Glucose and talc, therefore, play no part in the production of *polyneuritis gallinarum* which results from an exclusive diet of polished rice. (5) These experiments indicate that legislation or regulations against the sale of polished rice, based upon the fact that *polyneuritis gallinarum* results from feeding it as an exclusive diet, are not warranted. (6) The evidence here presented indicates that several other common articles of diet produce *polyneuritis gallinarum* as certainly as does rice, either polished or unpolished: in three instances these other foods produced the disease in quicker time than did rice. (7) There is, therefore, more argument against the sale of these common articles of diet, sago, Irish potatoes, and corn starch, than there is against the sale of rice, "polished" or "unpolished" milled or under-milled.

Perineal Abscess in a Typhoid Bacillus Carrier.—L. LEVY (*Deutsche medicinische Wochenschrift*, July 31, 1913) reports on the original illness of a patient which occurred at the age of fifteen in January, 1907. The patient remained in the hospital until August of the same year and was then discharged as a bacillus carrier inasmuch as the urine contained constantly typhoid bacilli. During the ensuing years the patient suffered considerable from urinary difficulties, and in 1911 he was refused enlistment in the army because of a purulent discharge from the urethra. In September, 1912, he was admitted to the hospital because of perineal abscess which, upon being opened, discharge thick, creamy pus containing typhoid bacilli in pure culture. The pus cavity connected directly with the urinary passage. The persisting urinary fistula was corrected by operation in February, 1913. The treatment of this case had been undertaken a number of times with urotropin but without result. That this man had been a serious cause of illness for those brought in contact with him is shown by the fact that in 1907, 9 of his associates came down with the disease; in 1908, 6 persons; in 1909, 4 persons; in 1910, 27 persons, and in 1911, 1 person.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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The Effect of Salvarsan on the Circulatory and Renal Systems.—ALVERENS (*Arch. f. exper. Path.*, 1913, Band lxxii) conducted experiments upon rabbits, and found that long-continued administration of salvarsan intravenously brought about a slight nephritis attributable to the arsenic contained. In the toxic doses, administered during a short time, marked fall of blood pressure and serious interference with renal function occurred, but lesions were not visible in the kidneys. If neosalvarsan were administered for a long period, nephritis was not clinically observed, although definite change could be demonstrated in the kidneys. If administered for a short time, the giving of neosalvarsan was less deleterious to the animals than salvarsan. If nephritis had been previously excited by cantharidin, rabbits showed marked sensitization to salvarsan, whereas if the nephritis had been caused by mercury or chromic salts, that is, were essentially tubular, no ill results were obtained till large doses were employed. Animals with aortic and tricuspid incompetence were treated, with the result that cases of tricuspid insufficiency with resulting congestion of the abdominal organs bore salvarsan worse than those affected merely by an aortic leakage.

Thrombosis in the Lymphatic Channels.—OPIE (*Jour. Med. Research*, October, 1913) details some interesting observations upon thrombosis and occlusion of lymphatics. Opie points out that in circulating blood, the blood platelets perform an important part by gathering at the site of an injury to the endothelium, so that fibrin is deposited upon the mass of platelets. Lymph from the thoracic ducts, on the other hand, coagulates very slowly because of the small quantity of thrombokinase present in it; the addition of blood or of lymph-tissue-extract brings about firm coagulation. There is thrombin present, but thrombokinase is deficient. It was thought likely that thrombosis might be produced by direct introduction of tissue-extract or tissue cells into the lymphatics, and this was done after ligation of the thoracic duct near its point of entry to the venous system. Tissue cells or tissue juices introduced into the mesenteric lymphatics will then produce a prompt thrombosis. It was noticed that in such a state edema occurs, but that there was a marked tendency to rapid formation of collateral lymphatic circulation. Further, it was noted that if occlusion of the duct was produced, followed by injection of bacteria into the circulating blood, thrombosis in the lymphatics occurred. A necrosis of cells in contact with the lymph stream favors thrombosis in the lymphatic vessels, because in this way thrombokinase is brought into contact with the circulating lymph. Bacteria

are potent in bringing about this effect, doubtless because they cause injury of the endothelial cells, and the suggestion is made that bacterial infection is successfully resisted partly by reason of a free flow of lymph which is rich in bactericidal substance. If the thoracic duct be occluded, or in fact any large lymphatic trunk, edema occurs which is relieved by the establishment of collateral circulation. In the experiments above mentioned, this was brought about in one case by formation of a new channel which entered the proximal part of the ligatured duct, and in another case by collaterals which ran to the right thoracic duct; while in some cases no such communication could be made out, but the edema was not widely spread. If occlusion of the thoracic duct and injury of the mesenteric duct be produced, chylous ascites may occur.

Paleopathology.—Prof. Ruffer (*Jour. Path. and Bact.*, October, 1913, xviii, No. 2) has coined this unusual word to embrace knowledge that may be gained as to the inroads of disease upon bodies preserved to us from ancient times. He has had an opportunity of studying the pathological lesions in Coptic bodies dating from the fifth century of the Christian era. The bodies were not mummies in the proper sense of the word, but owed their wonderful preservation to the dry sand and to salt. They were evidently for the most part Christians, and many were dressed in embroidered garments. The teeth were found very badly diseased; caries was common; pyorrhea alveolaris and periodontitis were frequent, and it is evident that little care was bestowed in life upon the teeth by the Copts; nor was there any evidence that dentistry was understood by them. Spondylitis deformans was frequent, usually localized to a few vertebræ. Hypertrophy of the middle turbinated bones was noted; enlarged spleens, supposed to indicate malaria, were also found. The histological observations will be given later.

Tubercle Bacilli in the Feces.—So much has been written about the presence of acid-fast bacilli in the feces of tuberculous and non-tuberculous persons, that it is a little difficult for the casual observer to know what he should believe with regard to the frequent presence of tubercle bacilli in the stools. Laird, Kite, and Stewart (*Jour. Med. Research*, October, 1913) have undertaken careful experimentation with a view to clearing up this vexed subject. Many observers have shown the presence of tubercle bacilli in the stools of tuberculous people. By some this has been credited to swallowing the sputum, and by others to the presence of ulcers in the bowels. Many acid-fast bacilli in the stools of animals and of human beings ill with various diseases have been reported, and in some cases it has been definitely stated that these were tubercle bacilli. Tubercle bacilli are sometimes found in the stools, while none can be demonstrated in the sputum, while in a large series of cases with bacilli in the sputum they were also capable of demonstration in the stools. A series of cases was reported in which tubercle bacilli were found in the stools of all of 100 patients who had tubercle bacilli in the sputum, and in more than 20 per cent. of 1000 other persons. The above mentioned authors at Saranac have examined a large number of persons, and have concluded that nearly all patients with tubercle bacilli in their sputum

also have tubercle bacilli in the feces; whereas very few persons who have no tubercle bacilli in the sputum have even acid-fast bacilli in the feces. In most cases where acid-fast bacilli appear in the sputum animal experimentation was performed with positive results; the feces which did not contain acid-fast bacilli were frequently examined by experimental inoculation of animals with negative results. The authors did not find acid-fast bacilli to any marked extent in the feces of those whose sputum did not contain tubercle bacilli, and their conclusion is that sputum frequently swallowed during sleep is the most likely explanation of the presence of these germs in the stools. The authors further go upon record as doubting the frequent presence of tubercle bacilli in the blood, a position which is the more tenable because good workers have repeatedly failed to obtain them from the blood.

The Bacteriology of Condensed Milk.—ANDREWES (*Jour. Path. and Bact.*, 1913, vol. xviii, No. 2) has examined a large series of samples of condensed milk with regard to bacterial content, a study which gains some importance when one considers that 50,000 tons of this product are imported into Great Britain in a year. In spite of the "villainous appearance of the stained sediment," none of the samples could be accused of containing pus; a high cell count with a percentage of polymorphs of over ninety ought to be present before the presence of pus could be determined. As to bacteria, the process of condensation appears, in many cases, to sterilize the milk, but a notable exception is in the case of staphylococcus, which finds in sweetened condensed milk, a medium that is almost differential. Andrewes does not absolutely condemn a milk that contains 250,000 cocci per cubic centimeter; nevertheless he thinks it would be safer to do so, and that efficient pasteurization should be performed before the milk is condensed and sweetened.

Arterial Lesions in Rheumatic Fever.—OSKAR KLOTZ (*Jour. Path. and Bact.*, October, 1913, vol. xviii, No. 2) has studied an interesting case of aneurysm of the ascending aorta found in a boy, aged six six years, with rheumatic fever. It was evident during life that the heart was seriously involved, and blood cultures gave a pure growth of streptococcus in short chains. In addition to the disease of the mitral and aortic valves, and much fibrinous deposit in the vicinity of the aortic opening, there was found in the ascending aorta, on the posterior surface, an aneurysm measuring $2\frac{1}{2} \times 2 \times 1\frac{1}{2}$ cm. Two-thirds of the circumference of the aorta was involved in this dilatation. Histological examination of the aortic wall showed that the external coat especially in the vicinity of the vasa vasorum were markedly affected. Infiltration was partly leukocytic and partly lymphocytic, and plasma cells were present. Nothing like abscess formation was found anywhere, but marked necrosis was observed in the areas of the muscular elements. In the sac, the adventitia and a small portion of media were reinforced externally by the pericardium. Fibrinous clot and its contained leukocytes were found in the interior of the sac. Streptococci were demonstrable in the affected tissues. The finding of so marked an arterial change in the course of rheumatic fever comes to us as a surprise, and yet there is no inherent reason why this should

be so. The development of aneurysm in rheumatic fever is like the process in syphilis, insofar as the inflammatory invasion begins in the vasa vasorum of the media and in the adventitia. The secondary intimal reaction with nodular thickening familiar in syphilis was not present. The reason that the bacterial invasion attacks the ascending aorta is as yet unexplained, but it is evident that the process is embolic, and is connected with the vasa vasorum in which fairly large masses of bacteria are lodged. Observations with reference to the effect of rheumatic fever upon the vessels come almost entirely from French literature, where for many years one has been able to find scattered reports. It would be well if closer observations were made with reference to the effect of such acute bacterial disease upon the arteries.

Anthracosis.—HAYTHORN (*Jour. Med. Research*, December, 1913, vol. xxix, No. 2) has published some interesting studies upon anthracosis, and the importance of this lesion on the course of other diseases. Contrary to general supposition, Haythorn finds that the upper air passages do not seem to be the portal of entry, for the epithelial layers do not appear to be invaded by soot particles. When carbon pigment in abundance was brought in contact with the mucosa of the mouth and upper air passages, he found no evidence of phagocytosis of such pigment higher than the lung alveoli. Large mononuclear cells are found in the alveoli, laden with pigment, or they may be found in the interalveolar or other lymph spaces. If pigment cells are seen in the deep layers of the bronchial mucosa, they are usually perivascular in position. Lymph channels of small and moderate size are often seen to be plugged by such cells, and there is ptosis, apparently out of proportion, great in amount. Haythorn thinks the pigment concontaining cell is not the lining cell of the alveolus, but is an endothelial cell, and, as such, is perhaps identical with the endothelial leukocyte of the blood. Experiments showed that the polynuclear leukocytes are unimportant as pigment phagocytes. Haythorn further thinks that pigment once ingested remains in the cell until disintegration frees it. The phagocytic cells wander into the lymph channels, and lodging there, may become surrounded by connective tissue. The importance of the process rests upon the frequent lymphatic obstruction that results, which is favorable to the localization of a tuberculous focus, and unfavorable to the resolution of a pneumonic area. The pigment-carrying cells appear to take their part in the formation of a tubercle, and the presence of pigment does not preclude the ingestion and phagocytosis of tubercle bacilli.

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